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Volume 18

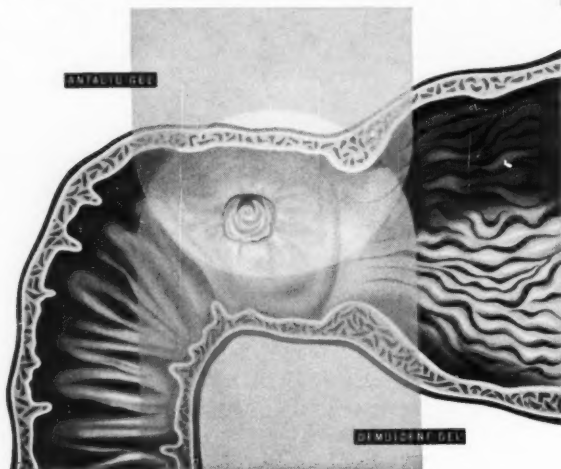
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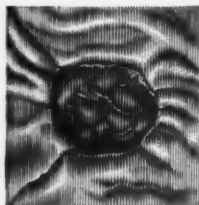


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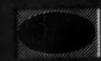


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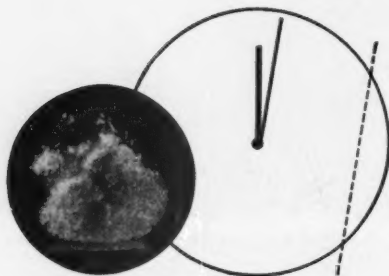
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EMERGENCY SURGERY IN MASSIVE HEMORRHAGE FROM HIGH LESSER CURVATURE ULCERS

FRANK J. RACK, M. D., Cleveland, Ohio.

THE PROBLEM OF massive hemorrhage from the upper gastro-intestinal tract is considerably simplified after the site of hemorrhage is determined. Usually this can be done quickly when radiological barium studies are carried out as soon as possible after the onset of bleeding, even during the bleeding phase (1,2). However, when the bleeding site is found to be ulceration above the mid-portion of the lesser curvature and when the patient fails to respond to transfusion and other medical measures and continues to hemorrhage, surgical intervention becomes imperative. Such a situation poses a difficult problem for the surgeon.

The patient is usually exsanguinated, is in the older age group and a poor risk for surgery. What should be the surgeon's plan of attack in such a situation? Should a high gastric resection including removal of the ulcer be done when such a procedure obviously will be technically difficult and prolonged? Or should some less radical procedure be utilized in consideration of the patient's poor condition and the increased mortality attendant to high resection? This may include gastrectomy in which the ulcer is left in situ, wedge excision of the ulcer or mere ligation of gastric vessels.

We have been faced with this problem on four different occasions at this hospital during the past 2 years and present our experiences with this situation.

CASE REPORTS

Case 1.—(#298777)—J. N., a 32 year old white male, was admitted to Cleveland City Hospital on September 8, 1948, because of hematemesis, tarry stools and weakness of 6 hours duration. There was a 10 year history of ulcer distress and perforation once.

Examination on admission revealed the patient to be in shock. The red blood count was 1.69 million with 5.5 grams of hemoglobin. 1000 cc of whole blood were given and the patient responded quickly. He was then started on antacids and frequent feedings and became free of abdominal pain. The red blood count rose to 2.6 million. However, on the fourth hospital day he suddenly had another massive hematemesis of about 1500 cc of bright red blood and went into shock. 1500 cc more of whole blood were given.

An emergency gastro-intestinal study was done as soon as the patient came out of the shock and questionable outpouching was noted high along the lesser curvature of the stomach as well as midway between the base and apex of the duodenal bulb. During the next 4 days the patient appeared to have stopped bleeding and the red blood count rose to 2.78 million.

On the 9th hospital day the patient developed massive hematemesis for the third time and again went into shock. 1500 cc of whole blood were given and the patient was taken to surgery. Under gas-oxygen-ether anesthesia an ulcer was found on the lesser curvature 3 cm from the cardia. Because of its high position the operator felt that gastrectomy with removal of the ulcer would entail too high a resection incompatible with patient's poor condition. For this reason a Polya type of resection was done leaving the ulcer in situ although the vessels along the lesser curvature including the left gastric artery were ligated.

The patient did well for 6 days post-operatively. On the 7th post-operative day, however, he vomited small quan-

Submitted June 30, 1950.

(From the Department of Surgery, Cleveland City Hospital and the School of Medicine, Western Reserve University)

ties of bright red blood but by the 12th post-operative day the red blood count had risen to 3.8 million. The patient remained asymptomatic until the 15th post-operative day when he began to vomit blood again and to deteriorate rapidly. The patient died on the 17th post-operative day in the midst of a massive hemorrhage. No autopsy was done.

Comment.—This patient was in the younger age group sustaining his first hemorrhage and there was little reason to believe that he would not stop bleeding spontaneously. However, after bleeding recurred for the third time during medical treatment emergency operation appeared justified in spite of the patient's poor condition. When the high position of the ulcer was ascertained the operator elected to do a sub-total Polya resection to avoid dissection and anastomosis high along the lesser curvature and in hopes that enough of the acid bearing portion of the stomach would be removed to allow for healing of the ulcer left in situ. But this failed to prove effective and the patient exsanguinated.

Case 2.—(#282394)—W. G., a 70 year old white male, was admitted to Cleveland City Hospital on February 1, 1949, because of pains in the abdomen, vomiting and tarry stools of 4 weeks duration. There was a 10 year history of indigestion.

Examination on admission was not remarkable except for benign enlargement of the prostate. The red blood count was 3.5 million with 12.5 grams of hemoglobin. The patient was placed on an ulcer routine empirically and during the next 11 days felt somewhat improved.

On the 11th hospital day the patient had a massive hematemesis, passed a tarry stool and went into shock. The red blood count dropped from 3.3 million to 1.5 million with 5.5



Fig. 1.—Radiograph made in Case 2 showing high position of ulcer along lesser curvature.

grams of hemoglobin and a hematocrit of 15%. Emergency studies of the upper gastro-intestinal tract revealed a high lesser curvature ulcer (Figure 1). The patient was given 3 units of plasma and 1000 cc of blood.

Nineteen hours after the onset of bleeding the patient was operated upon. Surgery was started under local procaine intercostal block anesthesia but the patient became completely uncooperative and it was necessary to revert to gas-oxygen-ether anesthesia. There was marked induration along the lesser curvature extending from the anterior to the posterior wall and gastrectomy revealed the presence of an ulcer high in this area. Frozen sections made from this area revealed no evidence of malignancy. Because of the patient's age and poor condition a wedge resection of the ulcer was done rather than a high resection.

About 12 hours post-operatively the patient developed atelectasis and this was treated by tracheal aspiration. A radiograph of the chest made on the 4th post-operative day revealed massive broncho-pneumonia on the left. Positive pressure oxygen was necessary to keep the patient comfortable. On the 6th post-operative day 1000 cc of whole blood were administered as supportive therapy. During the next few days the patient's condition, however, deteriorated steadily and on the 8th post-operative day the patient had a massive hemateme-sis and died.

Post-mortem examination revealed that the sutured wound representing the area from which the wedge had been excised had broken down and ulcerated with massive hemorrhage into the gastro-intestinal tract. The gastrectomy wound in the anterior wall of the stomach was well healed. Incidentally discovered was an undifferentiated carcinoma of the right upper lobe bronchus (small cell type) with metastasis to the tracheo-bronchial lymph nodes.

Comment—This patient developed massive hematemesia while on an adequate medical routine for ulcer. In a person aged 70 this is sufficient indication for emergency operation in spite of the patient's poor condition. Under such circumstances local anesthesia is much to be preferred but the patient's reactions made it necessary to use a prostrating general anes-

thetic. When the ulcer was found to be high on the lesser curvature gastrectomy to include removal of the ulcer would have required complete dissection of the indurated tissues along the lesser curvature and a Hofmeister resection. But the patient's condition did not seem to warrant such a prolonged procedure. The possibility of a malignant process had been excluded to a certain degree by the frozen sections and a wedge resection appeared to be an expedient procedure allowing for a quick attack on the bleeding ulcer. The patient's stormy course post-operatively was aggravated no doubt as the result of the prostrating general anesthetic used during operation. But nevertheless excision of the ulcer failed to prevent additional exsanguination.

Case 3.—(#298254)—F. H., a 56 year old white male, was admitted to Cleveland City Hospital on August 18, 1948, because of far-advanced pulmonary tuberculosis. Shortly thereafter two stages of a thoracoplasty were done but completion of this procedure was abandoned because of low vital capacity.

On April 7, 1949 the patient suddenly had a massive hematemesia and went into shock. The red blood count was 2.8 million. 500 cc of blood were given and the patient responded quickly. On the following day the patient had another massive hematemesia and again went into shock. 1000 cc of blood were administered with a satisfactory response. On April 9th an emergency gastro-intestinal study revealed a large peptic ulcer along the lesser curvature of the stomach (Figure 2). Because of the patient's far-advanced pulmonary tuberculosis, low vital capacity (49%) and dilatation of the ascending aorta suggestive of luetic aortitis surgery seemed to be contraindicated.

But on April 11th the patient again had a massive hematemesia and went into shock for the third time in four days. Emergency gastrectomy was then carried out, four days after the onset of bleeding. Intercostal procaine supplemented by nitrous oxide-oxygen and pentothal was used. A large ulcer was found along the lesser curvature of the stomach. Because of the ulcer's high position a Hofmeister type of resection was done with an ante-colic gastro-jejunostomy. The patient made an uneventful recovery and has remained asymptomatic.



Fig. 2.—Radiograph made in Case 3 showing large ulcer above mid-portion of lesser curvature.

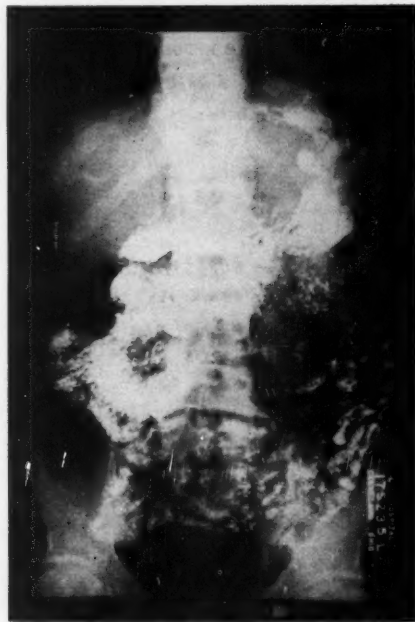


Fig. 3. Radiograph made in Case 4 showing ulceration along lesser curvature above mid-portion.

Case 4.—(#311933)—E. G., a 66 year old colored male, was admitted to Cleveland City Hospital March 6, 1950 because of repeated hematemesis of 24 hours duration. The patient was a chronic alcoholic but no history of ulcer distress was obtained. The physical examination was not remarkable except for prostatic hypertrophy. The red blood count was 2.5 million with 8.5 grams of hemoglobin and a hematocrit of 31%. An emergency gastro-intestinal series revealed a high lesser curvature ulcer (Figure 3). 500 cc of whole blood were given and the patient showed no further evidence of bleeding.

About 37 hours after admission the patient suddenly went into shock and had recurrent hematemesis. The red blood count dropped to 2.24 million and the hematocrit to 23%. A Levine tube was placed in the stomach and bright red blood aspirated in abundant quantities. An emergency gastrectomy was then carried out about 65 hours after the onset of bleeding. Intercostal procaine block supplemented by small quantities of pentothal and nitrous-oxide was used. A high lesser curvature ulcer was found and a Hofmeister resection done with excision of the ulcer and the formation of an ante-colic gastro-jejunostomy. The patient made an uneventful recovery.

Comment—Case 3 presented many contraindications to emergency gastrectomy and the attempt to do major surgery on this type of patient seemed heroic. However, it appeared the patient would exsanguinate unless emergency operation was done. Case 4 began to bleed again within 37 hours after being started on an adequate medical treatment. In a 66 year old patient this appeared to justify emergency surgery.

Both of these patients were successfully operated upon and an efficient definitive procedure completed, a high Hofmeister resection with removal of the ulcer.

CONCLUSIONS

The detection of a high lesser curvature ulcer causing massive hemorrhage uncontrollable by medical measures should not deter the surgeon from operating even in the very poor risk patient. Emergency high Hofmeister resections with removal of the ulcer can be done successfully with local and regional anesthesia. Although this type of resection prolongs the operating time and makes for a more difficult technical procedure the failure to remove both the ulcer and the acid producing portions of the stomach when dealing with massive

hemorrhage is fraught with danger from further bleeding.

The two deaths in this series were both due to the failure to carry out this principle. In one instance the ulcer was left in situ although gastrectomy was done. In the other patient only wedge resection of the ulcer was done. Both deaths were in patients who were given general anesthetics. In the poor risk patient a prostrating anesthetic adds to mortality and morbidity.

In the case of duodenal ulcerations the ulcer can readily be left in place during gastrectomy because several methods are available for covering the bleeding ulcer site. But in the case of gastric ulcers actual removal of the ulcer must be done to prevent recurrent hemorrhage after operation.

SUMMARY

1. Four cases of massive hemorrhage from peptic ulcers above the mid-portion of the lesser curvature are reported in which emergency surgery was carried out.
2. Two patients exsanguinated after surgery, one following gastrectomy in which the ulcer was left in situ, the other following wedge resection.
3. The emergency procedure of choice in these cases appears to be a high Hofmeister resection with removal of the ulcer under local anesthesia notwithstanding the patient's poor condition.
4. Two cases are reported in which this was done successfully.

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ROENTGEN FEATURES OF NON-MALIGNANT PERIAPPENDICEAL AND ILEOCECAL LESIONS

CHARLES GOTTLIEB, M. D., SAMUEL L. BERANBAUM, M. D. AND MILTON DORFMAN, M. D., New York, N. Y.

PERIAPPENDICEAL inflammatory lesions include a multitude of conditions with manifold clinical expressions. The commonest manifestation is undoubtedly the controversial entity of "chronic appendicitis." Apart from this entity, which will not be discussed, the Roentgen difficulties in differentiation between inflammatory and neoplastic lesions in this location present a major problem to a greater extent than elsewhere.

The cecum shows a great variation in location due to malrotation, and a great variation in appearance anatomically and physiologically. It is composed of two sacculations of unequal size. According to Cunningham there are three anatomical types: (1) the conical or fetal type, (2) the infantile type with the outer sacculaculum only slightly larger than the inner pouch, and (3) the adult type with an outer pouch much

larger than the mesial sacculaculum. The adult type is found in about 90% of cases. The fact that in humans the cecum is slow to assume its adult form may account for the large number of imperfectly developed cecums in adults.

The ileocecal valve is usually visualized roentgenographically on the mesial aspect of the cecum when observed in the AP projection. Normally, however, variations exist in the position of the ileocecal valve, its location depending largely upon the position of the cecum. If the cecum is partially rotated, the ileocecal entrance may be found on the lateral border or even towards the posterolateral margin of the cecum, making it extremely difficult to visualize roentgenographically. A mobile cecum may cause a great variation in the position of the ileocecal valve from time to time depending upon the degree of fullness of the cecum and the position of the patient.

The valve is formed by the oblique direction up-

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Department of Radiology, University Hospital, N. Y. U.,
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MARCH, 1951

ward and to the right of the terminal ileum which protrudes into the posteromedial wall of the cecum. The aperture is about one half inch in length and is horizontally placed between the prominent upper and lower mucosal lips. The configuration of the aperture is subject to great variation from time to time in the same patient and evidently varies in different persons. The valve-like lips which appear in the cadaver have not been observed in the unanesthetized subject (Alvarez 1940). Observation by Rutherford and others through a cecal fistula reveals a papilla about 1.8 cm. in diameter projecting about 1 cm. into the lumen of the cecum (Alvarez). Rhythmic changes in height and width of the papilla together with swaying movements associated with to and fro contractions of the terminal ileum were observed from time to time. When the patient was placed under deep anesthesia, the papilla relaxed and a slit-like valvular arrangement similar to that observed in the cadaver appeared. Rutherford found the sphincter to be tightly closed except during the entrance of chyme from the ileum.

The most important function of the sphincter is the prevention of ileal contents from entering the cecum too frequently, thus allowing time for digestion and absorption to be completed. Although there is no evidence of a well-developed muscular sphincter, the anatomic arrangement at the ileocecal juncture prevents the frequent regurgitation of cecal contents into the ileum. Observations made during the progress of the barium meal suggest that the regurgitation back into the ileum

is rare once it has passed ileocecal barrier. However, during the course of barium enema study, ileocecal regurgitation is frequently observed.

The sphincters of the colon from an anatomic standpoint may be divided into organic and functional types. They have been studied primarily by radiologists, whose names they bear (fig. 1). The sphincters are important physiologically in the mechanism of the digestive tract. They react by spastic contractures to lesions of the colon and other abdominal viscera. They do not necessarily act in the same way with a particular lesion, nor does the same sphincter always react to the same lesion. Sphincteric spasm is not a pathognomonic sign of an abdominal lesion, but is only a general sign of irritation. In our present discussion, the sphincter between the cecum and ascending colon, bearing the name of sphincter of Busi, is to be noted especially. Too often, this normal sphincter is given too much importance in a roentgen examination, and when persistent, is at times misinterpreted as a lesion.

The appendix is a tubular outgrowth springing from the inner and back part of the cecum about 1 to 1½ inches below the ileocecal orifice in the fetus and child as well as in the adult with infantile type of cecum. The appendix springs from a true apex, not from the inner and posterior aspect. The appendix, although it has been found in almost every possible situation in the abdomen, which its length allowed it to attain, generally runs in one of three chief directions: namely, (1) over the brim into the pelvis; (2) upwards behind the cecum; (3) upwards and inwards toward the spleen.

The taeniae of the cecum all spring from the base of the vermiform appendix.

Foreign bodies, although reputed to find their way very easily into the appendix are rarely found there after death. On the other hand, concretions or calculi, formed of mucus, feces, and various salts, are often present (coprolith). These are often visible on the plain roentgenogram, thus helping in the differential diagnosis in difficult cases.

The cecum, as stated, is the most variable in position of all the sections of the digestive tract. Because of the great variation in position of the cecum, it may be quite difficult to tell when the cecum is filled. Disease of the cecum may produce spasms just distal to it, beyond which barium may be forced with difficulty. Even when the terminal ileum is filled, it may at times present uncertainties. Of major assistance is the fact that the ileocecal valve entrance is never at the inferior tip of the cecum. This is well illustrated in the case illustrated in fig. 2—when on review of the films it was realized that the cecum was not entirely filled since the ileocecal valve was noted at the tip of the visualized large bowel. A re-examination with persistent emphasis to the ileocecal region then revealed an irregular filling defect of the cecum. The irritability, serrated margins, but most important the additional involvement of the terminal ileum enabled the correct preoperative diagnosis of an inflammatory lesion to be made, in contradistinction to a casual interpretation of a neoplasm on the first examination.

Whenever doubt persists as to the actual filling of the cecum, a re-examination by meal by mouth is of inestimable importance. This is illustrated by fig. 3. The proximal colon was not well visualized by contrast

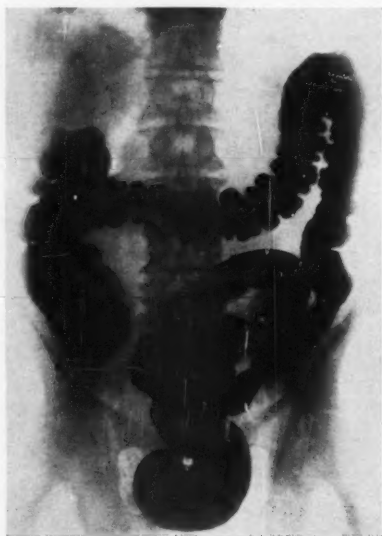


Fig. 1.—Normal colon filled with barium mixture showing the sphincters of the colon. The most proximal sphincter is that of Busi. This is frequently misinterpreted as an abnormal narrowing of the cecum. Note that it is proximal to the ileocecal area where the sphincter of Varolio is located. Proceeding distally from the ileocecal area are the Sphincter of Hirsch, Sphincter of Cannon-Boehm, Sphincter of Payr-Strauss, Sphincter of Balli, Sphincter of Moutier, and Sphincter of Rossi.

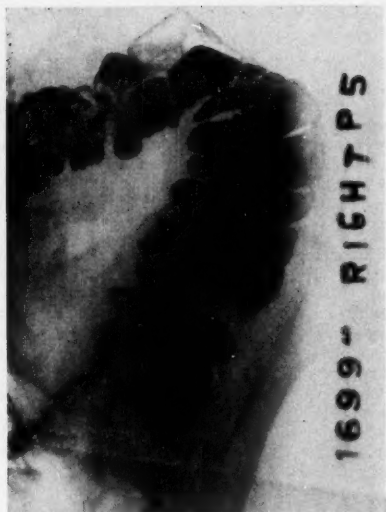


Fig. 2.—N. D. a 42 year old white female with alternating diarrhea and constipation, and abdominal cramps for four years' duration. The first examination (a) showed an irregularity at the ileocecal region. Since the ileocecal entrance is never at the inferior tip of the cecum, a re-examination was undertaken. In the second examination (b), the large filling defect of the cecum is better outlined. The only feature that differentiated this defect from a malignant defect was the associated narrowing of the terminal ileum with a large ulcer crater protruding from its superior aspect. At operation, a large hyperplastic inflammatory mass was found, with ulcerations and fistulous tract formation. The similarity of the Roentgen features to tuberculosis is noteworthy.

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Fig. 3.—A. S. a 34 year old white male with recurrent right lower quadrant abdominal cramps of about six months' duration, with the presence of a palpable mass. Barium enema examination was unsuccessful. A meal by mouth was therefore administered revealing an intussusception at the ileocecal region. The illustration taken at six hours shows the classical "bed spring" type of filling defect. This defect is characteristic of intussusception regardless of the underlying etiology. In this case it proved to be carcinoma of the cecum.

enema whereupon a gastrointestinal series was undertaken. A large intussusception at the ileocecal region was demonstrated only during the gastrointestinal examination.

Some examiners prefer not to have any ileocecal incompetency during an enema examination. After var-



Fig. 4.—Fig. 4 represents a filling defect due to fecal scybalae. The close similarity to a malignant defect is to be noted.

ied experiences we have found that if the patients have a regular meal prior to the examination, the incidence of ileocecal incompetency is decreased. Cleansing of the large bowel prior to examination is of course an absolute prerequisite. Otherwise the danger of misinterpreting feces for a true intraluminal defect is ever present (fig. 4). When in doubt a re-examination especially with a double contrast enema, will enable the correct diagnosis to be made.

The most frequent complication following an appendectomy is adhesions. By and large the diagnosis of adhesions is too frequently made. Limitation of mobility of the cecum during contrast enema is a frequent observation, often due to voluntary spasm. When in doubt, exposures taken in the upright help considerably.

Examination after the ingestion of barium is superior because voluntary spasm during an enema is no longer a factor. Serial radiographs in different positions (upright, prone, oblique) taken one after the other lend confirmatory evidence to the fluoroscopic findings.

If fluoroscopic and radiographic evidence of adhesions is not corroborative, a diagnosis of adhesions is hazardous. In spite of all these considerations, cecums which cannot be moved under the fluoroscope, are often found at operation to be perfectly free and mobile.

There is only one pathognomonic sign of adhesions,



Fig. 5.—C. R., a 21 year old white male with recurrent right lower quadrant pain after an appendectomy two years earlier. The kinking of the ileum observed, proven at operation, is the only pathognomonic sign of adhesions. The cobble-stone type of multiple filling defects in the ileum represents the normal mucosal pattern in children, and, as in this case, young adults. They are produced by the abundance of lymphoid tissue in the Peyer's patches. Later in life, the more usual parallel longitudinal mucosal pattern is noted.

viz. actual kinking or distortion of the course of the ileum (see fig. 5).

The cecal "filling defect" with or without a palpable mass, may at times present a most vexatious problem in the differentiation between neoplastic and benign inflammatory lesions. Carcinoma invades the wall, destroys the mucosa, protrudes into the lumen producing a filling defect. The degree of symmetry or asymmetry is of no diagnostic significance. There is usually a palpable mass, slight irritability, and often slight tenderness.

An inflammatory mass, whether it be specific or non-specific in character also may produce a filling defect. Round, smooth borders, with sharp outline favor an inflammatory abscess. On the other hand a defect with narrow canalization and overhanging edges is strong evidence for a neoplasm. The mucosal pattern outline may be destroyed as in neoplastic infiltration; but if it be intact, with only pressure defect, the diagnosis of an inflammatory lesion is on more certain grounds. A coarsening of the mucosal pattern accompanied by irritability and tenderness is again more in favor of an inflammatory process. Multiplicity of lesions, as well as individual lesions that are relatively long—all these factors suggest an inflammatory basis but are not pathognomonic. In no location in the gastrointestinal tract must there be a closer clinico-roentgen correlation than at the ileocecal region.

The difficulties encountered in a preoperative roentgen diagnosis are well illustrated in the accompanying cases briefly reported. Too frequently is the presence of a filling defect with or without a mass considered to be almost synonymous with a neoplasm. The cases presented all have a filling defect as a common denominator, yet none are neoplastic (excepting intussuscepting neoplasm). The multitude of benign ileocecal and periappendiceal lesions are well known. To outline a detailed description of all these conditions is beyond the scope of this paper. We merely wish to stress the frequency of the inflammatory filling defect and the manner in which an attempt at roentgen differential diagnosis is made.

The commonest inflammatory filling defect is secondary to an appendiceal abscess. The variation in anatomical location of the appendix (vide supra) results in different roentgen features. Most commonly the defect is eccentric on the medio-inferior aspect of the cecum as illustrated in cases 6a and b. This defect is usually smooth, clear cut and distinct. An attempt to study the mucosal pattern will show a normal outline with no destruction. Mucosal pattern studies are best made during fluoroscopy with graded pressure spot filming as the bowel is gradually filled. The expulsion film, as well as the double contrast with air help considerably.

The retrocecal appendix often presents major obstacles in diagnosis. This is especially well illustrated by the case in fig. 7, representing the findings of a filling defect, in the ascending colon yet with intact mucosal pattern with relatively smooth margins. Prior to this examination a perinephritic abscess had been drained. Laparotomy revealed a retrocecal appendix pointed towards the liver which had ruptured resulting in a hard inflammatory mass.



Fig. 6a.—A. P., a 50 year old practical nurse with a history of right lower quadrant abdominal pain and weakness of about six months' duration with an anemia and a palpable mass. The barium enema showed ileocecal spasm with a filling defect. Its smooth contours and its eccentric location on the medio-inferior aspect suggested its inflammatory character. At operation an appendiceal abscess was found.

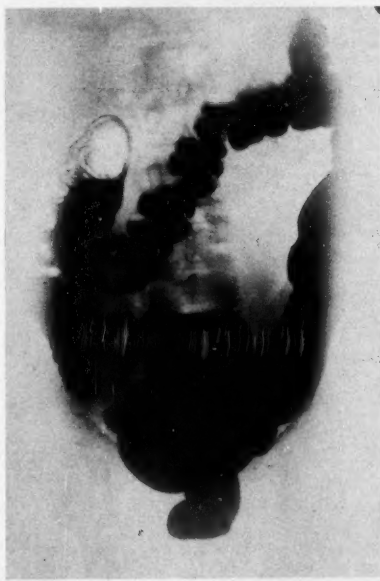


Fig. 6b.—L. S., a 32 year old white male with a right lower quadrant mass and anemia. The barium enema showed a

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smooth, eccentric intraluminal defect on the medio-inferior aspect, as well as the associated spasm of the ileum again suggests its inflammatory character, proven to be an appendiceal abscess.

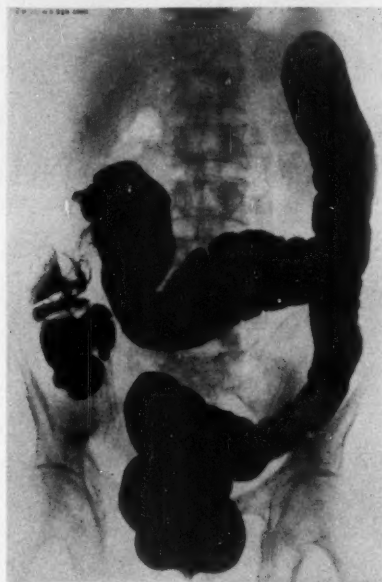


Fig. 7.—Sixty year old male who had been suffering from increasing pain in right side of back, temperature elevation, and anorexia of four months' duration. Intravenous pyelography was negative. A perinephritic abscess was drained 2½ months prior to colon examination. Drainage, anorexia and pain in back were continuous.

Barium colon examination disclosed a filling defect of the ascending colon. Note that the narrowed area does not have the rigid irregularity of neoplastic canalization, that the mucosal pattern is still intact, and that the superior and inferior borders of the defect are smooth without overhanging edges.

Laparotomy disclosed a retrocecal appendix pointed toward the liver. The appendix had perforated, and a hard, inflammatory mass surrounded the ascending colon.

Chronic inflammatory diseases of the ileocecal region commonly produce hyperplastic changes, which roentgenographically result in a filling defect. This is especially true in granulomatous lesions.

In regional ileitis the roentgen appearance will depend on the state of the pathologic process. Early, the lumen may be slightly encroached upon; the contour is irregular, the mucosal pattern is destroyed. Polypoid hyperplasia results in irregularly outlined translucent areas. Later, the wall becomes thickened resulting in a rigid tube little altered by peristaltic activity and the lumen becomes increasingly narrowed.

Concomitant with the changes in the ileum, the cecum may show deformity due to either spasm, or pressure against the inner border of the cecum by the inflammatory process in the ileum, or actual organic inflammatory disease of the cecum. This condition may be indistin-

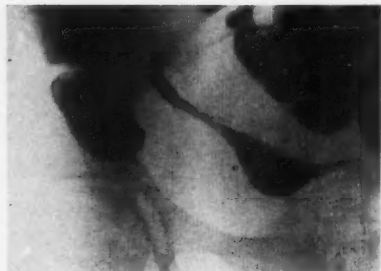


Fig. 8 (a & b)—Two examples of non-specific ileocolitis. In (a) the typical appearance of inflammation of the terminal ileum is observed, viz., narrowing and serrated mucosal margins. The associated smooth, eccentric filling defect on the medial aspect of the cecum due to associated hyperplastic inflammatory changes, often makes the differentiation from tuberculosis extremely difficult.

In (b) in addition to the ileocecal inflammatory changes with bud-like appearance of the contracted cecum, there is a further inflammatory narrowing of a large portion of the transverse colon. The multiplicity of the lesions in different locations, as well as the length of the individual lesion point to the inflammatory character of the lesions.

guishable from the roentgen appearance produced by tuberculosis (figs. 2 and 8a & b).

Multiplicity of lesions, the greater length of the individual lesion involvement of both cecum and ileum, serrated mucosal margins, with or without ulcerations—all these speak strongly for an inflammatory basis of the findings.

Amebic involvement occurs most frequently in the cecum. A small portion of ileum may be involved only

when there are an enormous number of amebae in the large intestine.

Roentgenologically, there may be no distinguishing features which permit exact differentiation of the deformities produced by amebic colitis from those resulting from idiopathic ulcerative colitis. The only finding of a suggestive nature is the preponderant susceptibility of the cecum to invasion. The granulomatous processes which may develop are indistinguishable from those that are nonamebic in origin. These lesions may closely simulate those produced by malignant infiltration, but as we have attempted to show, the filling defect in the cecum is often smooth in outline.

In the pre-granulomatous stage of amebic cecitis, the cecum may show nothing more than spasm, and distorted mucosal patterns. The demonstration of the parasites in the stool is the best positive manner to establish the diagnosis.

Tuberculosis usually starts in the ileocecal region. Indeed, the terminal ileum may be narrowed in such a manner as to be roentgenographically indistinguishable from non-specific granuloma, even to the extent of fistulous tract formation. As a rule, the cecum is





Fig. 9a & b.—Granulomatous lesions at the ileocecal region produce filling defects often indistinguishable from a neoplasm. In (a) a classical appearance of ileocecal tuberculosis is presented, with hyperplastic inflammatory changes consisting of a narrowed conical cecum, with serrated mucosal pattern and ulcerations. Fluoroscopically, the marked ileocecal spasm with difficulty in filling are important corroborative findings.

By the way of contrast in (b) a granulomatous eccentric filling defect is presented indistinguishable from a malignant infiltration. Amoebae in the stool established the diagnosis. Similar defects are observed in all granulomatous inflammatory lesions, more typically in amebiasis of the cecum.

simultaneously involved with the terminal ileum. Classically, the terminal ileum shows changes ranging from transient spasm and mucosal irregularity to complete loss of mucosal markings, narrowing, irregularity, and rigidity of the walls, and presence of an ulcer crater. The cecum, too, shows changes indicative of inflammation. Mucosal irregularities, spasm and deformity of shape, Stierlin's sign (a gap in the cecal shadow when the ileum and colon are filled) appear (figs 9a & b).

Recently the defects produced by a hypertrophied ileocecal valve, or ileal prolapse into the cecum have received added attention. The excellent studies by Fleischner and Bernstein on the normal roentgen appearance of the ileocecal valve will give this topic further impetus.

These authors illustrated the different variations in morphology encountered and described the distinct patterns, best observed by the application of pressure. The ileum is implanted into the medial colonic wall and

projects into the colonic lumen for 2 centimeters, which represents the valve itself. It is flattened forming a wedge-shaped lumen opening through a horizontal slit into the colon. The barium filled area between the lips varies from an elongated evenly calibered channel to a short plump cone.

Golden in 1943 first indicated that the ileocecal valve may become sufficiently enlarged to produce a filling defect on the roentgenogram. The protrusion of the mucosa is thought to be the result of eversion of the enlarged lips of the valve. Thus it would appear that hypertrophy of the valve and prolapse almost always occur together. These findings are normal variations, with the diagnosis being established by the intimate association of the mass to the valve. The smooth round



Fig. 10a & b.—B. S., a 57 year old white female with a questionable history of melena of about one year's duration, anemia, and periodic episodes of diarrhea. The barium enema with the colon distended with contrast media tended to obscure the defect, with persistent spasm pointing to the site of involvement. Mucosal studies, (a) best seen after evacuation, reveal a filling defect associated with spasm with a disturbed mucosal pattern, but with no actual destruction. The (b) double contrast examination best reveals the smooth globular polypoid intraluminal defect, with intact mucosal pattern, located anatomically at the ileocecal valve. The patient underwent an exploratory operation due to a difference of opinion regarding the significance of the above findings. Hypertrophy of the lips of the ileocecal valve was found with a slight degree of ileal prolapse.



Fig. 11.—A. S., a 69 year old white female, an arthritic patient at St. Barnabas Hospital for Chronic Diseases was investigated for constipation. Barium enema revealed an atonic colon. A smooth filling defect at the ileocecal valve as above illustrated, was considered due to a hypertrophied ileocecal valve. Three examinations (8/3/49, 10/7/49, and 4/8/50) showed the same defect, each time a perfect copy of the other, with no change. Operation has therefore been withheld.

contours, the lack of obstruction, local tenderness or other abnormality lends support to the final interpretation. Change in size or shape with prolapsed mucosa is a distinct help, when observed. Otherwise, the final

differentiation from neoplasm will rest on the clinical aspects of the case.

Hypertrophy of the ileocecal valve and/or ileal prolapse is quite rare. Hawley and Mithoefer reviewed the literature, found four cases and added two of their own. Our two cases (figs. 10 and 11) are included in this treatise both because of their rarity as well as the problem in differential diagnosis that is presented.

CONCLUSION

The differential diagnosis between an inflammatory and neoplastic mass is extremely difficult, and at times impossible. An illustrative review of roentgen features of the numerous pathological manifestations is presented with the realization that the final diagnosis depends on a correlation with the clinical findings.

In addition two cases of hypertrophy of the ileocecal valve and/or ileal prolapse are included.

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STUDIES ON ASCITIC FLUID IN PATIENTS WITH HEPATIC CIRRHOSIS, HEART FAILURE AND CANCER: RESULTS OF CEPHALIN CHOLESTEROL FLOCCULATION, THYMOL TURBIDITY, METHYLENE BLUE, QUALITATIVE AND QUANTITATIVE BILIRUBIN AND OTHER TESTS*

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THE THYMOL TURBIDITY and cephalin cholesterol flocculation tests are positive in the blood of patients with liver cell damage. This paper presents the results of these and other liver function tests carried out on ascitic fluid and on the blood of the same patients.

METHODS AND RESULTS

Cephalin cholesterol flocculation tests.

The cephalin cholesterol flocculation test with ripened emulsion as described by Hanger-Mateer (21), was performed on 45 specimens of ascitic fluid from 40 patients suffering from hepatic cirrhosis, heart failure or

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cancer. The test was read at 48 hours, and borderline tests (+) were considered "negative."

The test was "positive" in all 27 ascitic fluid specimens from 25 patients with cirrhosis of the liver: ++ in 70.4 percent, +++ in 22.2 percent, +++ in 7.4 percent (table 1). In the blood of these patients, the cephalin cholesterol flocculation test was "positive" in 25 of 26 specimens; +++++ in 68 percent, +++ in 24 percent, ++ in 8 percent, (table 1). In the remaining patient (Exp. No. 22) the blood cephalin cholesterol test was negative. Eight of nine specimens of ascitic fluid from 7 patients with congestive heart failure gave a positive cephalin cholesterol flocculation test, whereas the blood gave a positive test in only 5 of 9 specimens from the same patients (table 2). The percentage of positive tests in ascitic fluid from patients with peritoneal carcinoma was 78 percent, whereas the test on the blood from the same patients was positive in 56 percent (table 2).

THYMOL TURBIDITY TESTS

The thymol turbidity test was performed on 43 specimens of ascitic fluid from 38 patients. The test was considered positive when more than 3 units were found. The ascitic fluid in 24 patients with hepatic cirrhosis was uniformly negative (table 1). In the blood of the same patients, the results of the thymol turbidity test were in striking contrast, namely 83 percent positive (3.1 units to 35 units, table 1).

The thymol turbidity test in the ascitic fluid of patients with heart failure was negative with 1 exception (4.4 units) and in the ascitic fluid of patients with peritoneal cancer all tests were negative (table 2). The thymol turbidity test in the blood of the same patient revealed that of 7 tests in heart failure patients, 2 were positive and of 6 tests in cancer patients, 1 was positive (table 2).

METHYLENE BLUE TEST

The methylene blue test of Franke (1.2.) for bilirubin was negative in 39 of 41 ascitic fluids of all groups, although the quantitative bilirubin test (van den Bergh) revealed in these negative specimens a considerable content of bilirubin in many of them (0.3 mg. percent to 2.1 mg. percent, table 3). The qualitative "direct diazo reaction" (see below) in ascitic fluids with negative methylene blue tests was either "delayed" or "biphasic" (table 3). In the two specimens of ascites giving a positive methylene blue test (5 drops and more of the methylene blue solution had to be added to turn the green color into blue), the "direct diazo reaction" was "prompt" and the bilirubin content was higher (2.5 mg. percent and 4.2 mg. percent, table 3).

QUALITY AND QUANTITY OF BILIRUBIN

The "direct diazo reaction" was studied in 44 specimens of ascitic fluid of all 3 groups. To 2 cc. of ascitic fluid, 2 cc. of diazo reagent were added, and the appearance and speed of development of the purple-red color were watched. The "direct diazo reaction" was "prompt" in only 3 specimens, "biphasic" in 9 specimens and "delayed," usually incorrectly called "direct negative" or "indirect (3,4,5), in 32 specimens. In 12 patients the "direct diazo reaction" and the total bilirubin in the ascitic fluid was compared with the "direct diazo reaction" and the total bilirubin in the blood of the same patient (van den Bergh method). The results are listed in table 3. There was in the majority of the cases a striking discrepancy between the amount of total bilirubin in the blood and in the ascites (see exp. No. 7, 9, 12), and often a difference of the direct diazo reaction. In only two instances was the ascitic fluid bilirubin content higher than the blood bilirubin. In four cases the direct diazo reaction was "prompt" in the blood, while "biphasic" or "delayed" in ascitic fluid, and in one instance, "biphasic" in the blood and "delayed" in the ascites.

UROBILINOGEN AND CHOLIC ACID TEST

The urobilinogen test was negative in 44 of 45 specimens of ascitic fluid of all groups. One ascitic fluid (hepatic cirrhosis with jaundice) gave a ++ urobilinogen test to a dilution of 1:20. The modified Hay test for cholic acids (2) was negative in all 44 examined specimens of ascites.

SPECIFIC GRAVITY AND RIVALTA TEST

The specific gravity of the ascitic fluid and the Rivalta test—development of a cloudy precipitation when a few

TABLE I

Exp. No.	Prot. No.	ASCITIC FLUID		BLOOD	
		Cephalin Flocculation Test	Thymol Turbidity Test	Cephalin Flocculation Test	Thymol Turbidity Test
1	1	++++	—*	—	—
2	4	++++	0.3	+++	3.8
3	6	++	2.4	+++	24.9
4	7	++++	1.4	++++	5.0
5	7	++++	0.4	++	—
6	8	++++	1.3	++++	5.6
7	9	++++	0.8	++++	3.1
8	11	++++	2.0	++++	2.8
9	13	++++	3.0	++++	35.0
10	14	++++	0.6	++++	1.5
11	16	++++	0.7	++	—
12	16	++++	0.6	++++	5.6
13	18	++++	0.6	++++	15.0
14	22	++++	1.5	++++	8.2
15	23	++++	2.1	++++	3.6
16	24	++++	0.9	++++	4.5
17	25	++++	0.6	++++	7.2
18	26	++++	0.2	++++	3.9
19	27	++++	0.5	++++	2.0
20	28	++++	0.2	+++	21.0
21	32	++++	1.6	++++	3.3
22	33	++	0.8	+	4.5
23	34	++++	0.3	++++	3.1
24	37	++++	0.8	++++	4.8
25	38	++++	0.4	++++	4.4
26	39	++++	2.5	++++	7.5
27	40	++++	1.6	++++	1.7

Results of the cephalin-cholesterol flocculation test and the thymol turbidity test performed on ascitic fluid and on blood of patients with hepatic cirrhosis.

—* The test was not performed.

drops of ascitic fluid are added to a very dilute solution of acetic acid (1 drop glacial acetic in 100 cc. water) are often used for the differential diagnosis between exudates and transudates. In transudates (hepatic cirrhosis, cardiac failure) the specific gravity should range from 1.008 to 1.015 and the Rivalta test should be only slightly positive or negative. In exudates the specific gravity is supposed to range from 1.018 to 1.025 and the Rivalta test to be strongly positive. In 18 of 21 ascitic fluids from patients with hepatic cirrhosis the specific gravity ranged between 1.005 and 1.015; in the remaining three it ranged from 1.016 to 1.031. In 6 ascitic fluids from patients with congestive heart failure the specific gravity was 1.015 and 1.022. In 6 specimens of carcinomatous ascites 3 ranged from 1.005 to 1.012 and 3 from 1.022 to 1.028. The Rivalta test in instances of hepatic cirrhosis was negative in 9, + in 6, +++ in 12 of the 27 specimens. In 7 specimens of cardiac failure 3 were +, 4 ++; in cancer 1 was negative, 1 +, 6 +++ to ++++.

COMMENT

In hepatic cirrhosis a striking parallelism between the results of the cephalin cholesterol flocculation test in the ascites and in the blood of the same patient was found.

The figures of 96 percent positive cephalin cholesterol flocculation tests in the blood of patients with cirrhosis of the liver compare favorably with the 98.5 percent of positive tests found by Wade and his co-workers (9) and the 100 percent positive tests found by Pohle and Stewart (14).

In several instances the cephalin cholesterol flocculation test in the ascites was somewhat more positive than in the blood. In cases of suspected hepatic cirrhosis with a doubtful cephalin cholesterol flocculation test in the blood the test should also be performed with the ascitic fluid. Hanger and his co-workers (6) and sev-

eral other authors (7-10) believe that the cephalin cholesterol flocculation test is caused by an increase of globulin and of a substance accelerating the flocculation combined with a diminution of the albumin below the level necessary to inhibit the reaction. The blood proteins are considered to pass unchanged from the blood through the capillary membranes and the peritoneum into the ascites (cf. Mensch and Banks (11)). According to Hanger's theory of the cephalin cholesterol flocculation test, one should conclude that in the ascites of these patients the albumin content was lower and the globulin content higher, i.e., the albumin/globulin ratio as low or lower than in the blood. This, however, contrasts with the finding of Myers and Keefer (12) that in ascites of hepatic cirrhosis the albumin/globulin ratio was higher than in the blood because a larger portion of albumin has passed into the ascitic fluid, a fact later confirmed by Roche, Olmar and Samuel (13).

There is an approximate parallelism of the cephalin cholesterol flocculation test in the ascites and in the blood of patients with heart failure and with cancer. The high percentage of positive cephalin cholesterol flocculation tests in the ascites of both these groups show that this test is of no value for the differentiation of transudates and exudates. Jetzler (15), however, reported that the Takata Ara test, probably also based on changes of the albumin/globulin ratio, is positive in ascites of hepatic cirrhosis but negative in cardiac and carcinomatous ascites.

The results with the thymol turbidity test in the ascites and in the blood of patients with hepatic cirrhosis, heart failure and cancer are in striking contrast to the results with the cephalin cholesterol flocculation test. According to MacLagan (16), a positive blood thymol turbidity test is due to the presence of a globulin-phospholipid complex. Similar observations were made by McCord and his co-workers (17). Kunkel and Hoagland (18) believe that the combination of an increased γ globulin with a lipid

TABLE II
CONGESTIVE HEART FAILURE

Exp. No.	Prot. No.	Ascitic Fluid		Blood	
		Cephalin Flocculation Test	Thymol Turbidity Test	Cephalin Flocculation Test	Thymol Turbidity Test
1	2	negative	—*	—	—
2	15	+++	0.4	+	—
3	17	+++	0.3	—	0.8
4	29	++++	1.0	++++	2.0
5	30	++++	2.0	++	2.5
6	31	++++	2.9	+	1.6
7	31	++++	4.4	++++	4.4
8	31	++++	1.1	++++	0.8
9	35	++++	2.5	++++	4.2
PERITONEAL CARCINOMATOSIS					
1	5	+	1.0	negative	3.8
2	5	+++	2.0	+++	—
3	10	+++	0.4	++	1.4
4	12	++	0.6	+	—
5	19	+	0.6	+	1.1
6	20	++++	1.3	+++	—
7	21	++	0.3	+++	1.6
8	36	++++	1.6	+++	3.0
9	41	++++	0.6	+	0.3

Results of the cephalin-cholesterol flocculation test and the thymol turbidity test performed on ascitic fluid and on blood of 7 patients with congestive heart failure and 8 patients with peritoneal carcinomatosis.

—* The test was not performed.

complex associated with β globulin is necessary for a positive thymol turbidity test. We must conclude that the phospholipids present in the blood of the cirrhotic and other patients in such quantity to give a positive blood thymol turbidity test cannot pass to the peritoneal cavity in sufficient amount to make the thymol test positive in the ascitic fluid. The globulins, however, pass through, causing a positive cephalin cholesterol flocculation test in the ascitic fluid of hepatic cirrhosis, heart failure, cancer as described above.

The 83 percent positive blood thymol turbidity tests in hepatic cirrhosis concurred well with the cephalin cholesterol flocculation tests in the blood of these patients. However, considerable differences were found in the patients with congestive heart failure and cancer. In these groups, the cephalin cholesterol flocculation test in the blood was positive in 56 percent. The blood thymol turbidity test, however, was positive in only 23 percent (table 2). The thymol turbidity test would seem to correspond better with the clinical picture in those patients than the cephalin cholesterol flocculation tests. It would appear that in questionable cases of liver damage reliance on the cephalin flocculation test alone is not justifiable and that other well founded liver-function tests should be carried out. Since the methylene blue test for urine bilirubin is considered very sensitive, it was surprising that this test was negative in 95 percent of the examined ascitic fluid specimens, although in many a considerable amount of bilirubin was demonstrable with the van den Bergh method. The fact that in the two specimens with a positive methylene blue test the "direct diazo reaction" was "prompt" while in all the methylene blue negative specimens it was "delayed" or "biphasic" is consistent with the interpretation that only "free bilirubin" (prompt) gives a positive methylene blue test. "Bound bilirubin" (delayed, biphasic) does not seem to react with methylene blue in ascitic fluid.

The comparative studies (table 3) of the quantity and the quality of the bilirubin in the blood and in the ascites revealed that blood bilirubin undergoes changes while it passes from the blood to the peritoneal cavity. In agreement with previous observations (19,20) there is considerably less bilirubin in the ascites than in the blood. In the 2 specimens of ascites in which the bilirubin content was higher than in the blood the ascites was bloody and perhaps local formation of bilirubin occurred. The difference in the quality

of the bilirubin in the ascites and in the blood of the same patient, i. e. the change of the reaction, often from "prompt" to "biphasic" or even "delayed" is unexplained.

SUMMARY

The cephalin cholesterol flocculation test, the thymol turbidity test, methylene blue, bilirubin, direct diazo reaction, Hay test, urobilinogen test, specific gravity and Rivalta test, have been carried out on the ascites and blood of 40 patients with cirrhosis of the liver, congestive heart failure and peritoneal carcinomatosis.

The cephalin cholesterol flocculation test was "positive" in 100 percent of specimens of ascitic fluid of hepatic cirrhosis. In the blood of the same patients this test was "positive" in 96 percent. In ascites caused by heart failure "positive" tests were present in 89 percent, and in ascites caused by cancer in 78 percent. In each of these two groups the blood test was "positive" in 56 percent.

In contrast, the ascitic fluid thymol turbidity test in patients with hepatic cirrhosis was negative in all instances while in the blood of the same patient, this test was positive in 83 percent. In congestive heart failure and peritoneal carcinomatosis the ascitic fluid thymol turbidity test was negative in all but one instance, whereas the blood thymol turbidity test was positive in approximately one-quarter of the same cases. The significance of the contrasting results of both tests has been discussed.

Only 2 of 4 specimens of ascitic fluid gave positive methylene blue tests, although in many specimens the van den Bergh test showed a considerable amount of bilirubin present. The direct diazo reaction in these two specimens was "prompt," whereas in other specimens giving a negative methylene blue test "delayed" or "biphasic" reactions were observed.

The changes of the quantity and the quality (direct diazo reaction) of the bilirubin during the passage from the blood to the ascites have been reported and discussed.

The Hay test for cholic acids was negative in the 44 examined specimens of ascitic fluid of all groups. Similarly, in the same specimens the urobilinogen test was negative with one exception.

Studies of the specific gravity and Rivalta test of ascitic fluid of all groups revealed that these tests have

TABLE III

Exp. No.	Prot. No.	Diagnosis	Ascitic Fluid		Blood		
			Total Bilirubin Mg. %	Direct Diazo Reaction	Methylene Blue Test	Total Bilirubin Mg. %	Direct Diazo Reaction
1	4	Cirrhosis	0.3	delayed	neg.	1.6	biphasic
2	13	Cirrhosis	0.3	biphasic	"	1.2	biphasic
3	22	Cirrhosis	2.5	prompt	+	6.8	prompt
4	25	Cirrhosis	0.8	biphasic	neg.	5.3	prompt
5	26	Cirrhosis	0.4	delayed	"	0.5	delayed
6	27	Cirrhosis	0.3	delayed	"	0.5	delayed
7	28	Cirrhosis	0.8	delayed	"	12.6	prompt
8	32	Cirrhosis	1.1	biphasic	"	1.5	biphasic
9	33	Cirrhosis	2.0	biphasic	"	9.7	prompt
10	36	Cancer	1.5	delayed	"	0.3	delayed
11	40	Cirrhosis	2.1	biphasic	"	1.9	prompt
12	42	Cirrhosis	4.2	prompt	+	15.2	prompt

The methylene blue test and the quantity and quality of the ascitic fluid and blood bilirubin.

but limited value in the differentiation of exudates and transudates.

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AN EVALUATION OF FINDINGS IN GIARDIA INFESTATION

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ALTHOUGH *GIARDIA LAMBLIA* is frequently found in man, its pathogenicity and etiologic significance in patients with chronic diarrhea or other gastrointestinal complaints is difficult to evaluate. Recent surveys of approximately 25,000 ambulatory patients in the South have shown the incidence of infestation with this parasite to be as high as 14 to 16 per cent (1). When the parasite is found on stool examination in a patient with gastrointestinal complaints, its relationship to symptoms is of considerable interest and importance.

A review of the literature reveals that disease of almost every portion of gastrointestinal tract has been attributed to *Giardia*. These disorders have included gastritis, symptoms resembling peptic ulcer, the occurrence of jaundice, acute cholecystitis, epidemic diarrhea, dysentery and even manifestations of pancreatic insufficiency (2-8). Studies on experimental animals seem to indicate that the parasite may play a role in the production of such symptoms (1,8). Other reports have indicated that the parasite has little clinical significance in man, except perhaps in isolated instances (10,11,12).

The diagnosis is readily made when the parasite or

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cyst is demonstrated by microscopic examination of material obtained from duodenal drainage or from freshly passed liquid or semiliquid stools. These may be obtained by saline purgation, if necessary. Concentration techniques are of value only in identification of the cyst forms, since the trophozoites are killed by hypertonics solutions.

The trophozoite is pear shaped, coming to a point posteriorly and averaging 14 microns in length and 7 microns in width. It is motile, colorless, and finely granular. There are four pair of flagella. At the anterior end, on the ventral surface, is a large sucking disk by which it attaches itself to the mucous membrane. The parasites are located predominantly in the small intestine, and are most numerous in the duodenum. They are transmitted by the ingestion of contaminated food or water, in essentially the same fashion as *Endamoeba histolytica*.

CLINICAL STUDY

During the three year period from January 1, 1947, through December 31, 1949, the parasitology laboratory of the Bowman Gray School of Medicine performed by direct examination, and zinc sulfate flotation technique, a total of 5,399 stool examinations, on 2,522 patients seen in the North Carolina Baptist Hospital.

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Seventy-eight patients, or 3.1 per cent, were found to have *G. lamblia*. The data reported below were obtained from 59 of the above patients for whom adequate records were available.

Although approximately equal numbers of males and females were examined, 71 per cent of the infestations were found in males. Fifty-four per cent of the patients were less than 14 years of age, but only 25 per cent of the stools examined were from the pediatric wards.

Gastrointestinal complaints were present in only 23 patients, or 40 per cent. In order of frequency, they were as follows: abdominal pain (17), diarrhea (15), and abdominal pain and diarrhea (10). The abdominal pain had no constant location or character, and was never severe nor incapacitating. Weight loss, blood in the stools, fever, nausea, and vomiting did not occur unless some other disease was also present.

Of the 23 patients who harbored *Giardia* and had gastrointestinal complaints, 14 had other associated disorders which can produce abdominal pain and diarrhea. There were six instances of amebiasis, two of polyposis, and one each of malnutrition, carcinoma of the cervix, rectal abscess, esophageal hiatus hernia, irritable colon, and strongyloidiasis.

Thirty-seven patients who were infested with *Giardia* had no other intestinal parasites. Six had *Endamoeba histolytica*, 5 had *Ascaris*, 3 had hookworm, and 1 *Strongyloides*. Seven had a mixture of *Escherichia coli* and *Endolimax nana*.

ACCESSORY DATA

In no patient with a hemoglobin of less than 12 Gm. could the anemia be attributed directly or indirectly to *Giardia* infestation. In those patients harboring *Giardia* alone the percentage of eosinophils averaged 3.2 per cent, and the leukocyte count 6,200.

Ten patients were examined by the sigmoidoscope. Three had punched out lesions which yielded *E. histolytica* on smears, but *G. lamblia* was not identified. There was one instance of polyposis and one of non-specific idiopathic ulcerative colitis.

Eight patients had barium studies of the colon. Seven of these examinations were reported as normal, and one revealed loss of haustrations in the transverse colon and some irregularities in the lower descending colon. This patient was subsequently found to have *E. histolytica*. Three patients had roentgen examination of the stomach and duodenum, which were reported as negative. Cholecystograms were done in 2 patients who had symptoms suggestive of chronic cholecystitis. Both were negative.

Routine examination of the stool revealed *Giardia* in an 8 year old boy who was hospitalized for bacterial meningitis and who had no gastrointestinal symptoms. He expired two weeks later, and postmortem examination showed the gallbladder and small bowel to be normal.

TREATMENT

Eight patients with giardiasis, six of whom had gastrointestinal complaints, were treated with Atabrine. The *Giardia* disappeared from the stools of all these patients, and the 6 with gastrointestinal complaints showed

clinical improvement. In 2 of these, however, the improvement was transient. One returned later with proctoscopic and roentgenologic evidence of chronic idiopathic ulcerative colitis, and the other with amebiasis. In one patient, whose chief complaint was pruritus ani, disappearance of the parasite from the stool failed to produce any clinical improvement.

There were 5 patients in whom *Giardia* was demonstrated by a single stool examination and who received no treatment. When these patients returned for re-evaluation, parasites could not again be demonstrated. In 4 patients who had *E. histolytica* and *Giardia*, both parasites disappeared following treatment for amebiasis with carbarsone and chloroquine, or Diodoquin and emetine.

COMMENT

Where duodenal drainage or routine examination of liquid stools is performed in patients with gastrointestinal complaints, trophozoites of *G. lamblia* are frequently found. Stool examinations performed over a three year period by the parasitology laboratory of the Bowman Gray School of Medicine showed the parasites to be present in 3.1 per cent (78) of 2,522 patients. Trophozoites were identified in one-third of these cases. Thirty-seven patients had *Giardia* alone. Fifteen patients were also infested with *E. histolytica*, *Ascaris*, hookworm, or *Strongyloides*. The higher incidence of infestation found in males can probably be attributed to the fact that men more often eat away from home, possibly in less hygienic conditions, and hence are more likely to be exposed to the parasite.

No clear-cut clinical picture was presented by the group harboring *Giardia*. Only 40 per cent of the patients had associated-gastrointestinal complaints. These usually consisted of generalized abdominal discomfort, diarrhea, or both. Accessory laboratory studies, which included blood counts, cholecystograms, and roentgen examinations of the stomach, small intestine and colon, were of no diagnostic significance. Anemia and eosinophilia were not found. Sigmoidoscopy was helpful in disclosing associated diseases such as amebic and chronic ulcerative colitis, but not in the diagnosis of *Giardia* infestation. The majority of the patients who had definite gastrointestinal signs and symptoms usually had pathologic findings other than *Giardia* which have accounted entirely for their complaints.

Giardia disappeared rapidly from the stools of all patients who were given Atabrine. In two instances such treatment was helpful in disclosing another gastrointestinal disorder which was the primary cause for the presenting complaints. It is of interest that in several patients to whom no treatment was given, stool examinations repeated at a later interval no longer revealed *Giardia*. This finding suggests that the parasite may often disappear from the gastrointestinal tract without specific therapy.

From this study it would appear that *G. lamblia* is a common and usually nonpathogenic inhabitant of the human gastrointestinal tract. In the presence of anatomic defects or other pathologic processes, it may act as a secondary factor in producing gastrointestinal symptoms, particularly if the parasites are present in large numbers. There is no actual evidence that *per se* it can invade tissue. However, when it is found by stool examination or duodenal drainage, particularly if

gastrointestinal symptoms are present, treatment is indicated.

Carbarsone, chiniofon, and neoarsphenamine have been reported to be effective in the treatment of *Giardia* infestations, but they are potentially toxic agents. Atabrine, when administered in doses of 100 mg. three times a day for five days in adults and 50 mg. three times a day for three days in children, is safe and simple, and is 90 to 100 per cent effective.

SUMMARY

Giardia lamblia was present in the stools of 78 out of 2,522 unselected patients studied at the North Carolina Baptist Hospital over a three year period ending December 31, 1949.

Gastrointestinal complaints, most frequently pain and diarrhea, were present in 40 per cent of the infected patients.

Accessory laboratory studies, including blood counts and roentgen studies of the gastrointestinal tract and gallbladder, were of no diagnostic aid.

The patients who had blood in the stools, anemia, fever, weight loss, or other systemic manifestations usually had other findings besides *Giardia* to account for their complaints.

Giardia infestation is common, but usually produces few or no symptoms. It can be rapidly eliminated with Atabrine, and may disappear spontaneously.

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METABOLIC STUDIES IN GAVAGE AND PARENTERAL FEEDING DURING PROLONGED NARCOSIS THERAPY*

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THE NUTRITIONAL DATA obtained from a study of twenty-six patients who were subjected to continuous sleep for four to twenty-three consecutive days (an average duration of narcosis of 17.5 days) in the treatment of various psychiatric disorders are reported. The narcosis was uninterrupted and nutritional elements were administered by either gavage or parenteral routes. The desired narcosis was obtained by the rectal administration of Cloetta's mixture (1), a combination of hypnotic agents.*

These observations were made in the course of a study** of continuous sleep treatment in which the prevention of pneumonia was a principal objective. Previous use of the treatment revealed an incidence of pneumonia of forty-one per cent in a series of thirty-four cases. One of the possible factors in the production of pneumonia in these patients was aspiration during gavage. The study was designed,

*Cloetta's Mixture — Composition: Paraldehyde, 0.4864 Gm., Amylenhydrate, 0.1593 Gm., Chloral hydrate, 0.1157 Gm., Ethyl alcohol (92%), 0.1747 Gm., Isopropylalyl Barbituric Acid, 0.0409 Gm., Digalin, 0.0330 mg., Ephedrine HCL, 2.4600 mg.

***Continuous Sleep Treatment, a paper presented at the 105th Annual Convention of the American Psychiatric Association in Montreal, Canada, May 26, 1949, by John S. Clapp, M. D. and Earl A. Loomis, Jr., M. D. and to be published in the *American Journal of Psychiatry*.

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therefore, so that one half of the cases were fed by gavage, while the remaining patients were nourished by non-gavage methods.

The gavage group received 800 cc. of formula***, one liter of five per cent glucose in water, and one liter of tapwater. This was divided and administered in two or more gavages daily and provided 1459 calories.

The group not on gavage therapy received two liters of Aminosol (R), five per cent W/V with dextrose† intravenously, and 800 cc. of five per cent glucose in water either intravenously or subcutaneously providing 960 calories. Even though this caloric intake is not adequate to meet the daily needs, Elman (2, 3) states that a positive nitrogen balance is maintained without physiologic impairment through use of an intravenous mixture of equal parts of 100 Gm. of glucose and 100 Gm. of hydrolyzed protein. He (4) further states that about one half of the nitrogen in amino acids is utilized, the remainder being deaminized and used as a source of calories.

***Gavage Formula — Composition (per 800 cc.): Calories, 1269, Carbohydrate, 105.5 Gm., Protein, 47.5 Gm., Fat, 73.0 Gm., Salt, 5.0 Gm., Vitamin A, 5.8 I.U., Thiamine, 0.7 mg., Ascorbic Acid, 34.4 mg., Vitamin D, 25.9 I.U., Riboflavin, 1.4 mg., Nicotinic Acid, 5.0 mg.

†Aminosol with dextrose supplied through the courtesy of Abbott Laboratories, North Chicago, Illinois. Each liter contains: Calories, 400; Carbohydrates, 50 Gm.; Protein, 50 Gm.

Approximate Essential Amino Acids and Glutamic Acid
Grams per liter Per cent Calculated to 16% Nitrogen

3.0	Arginine	7.0
1.1	Histidine	2.5
3.5	Lysine	7.8
0.3	Tryptophane	0.8
1.5	Phenylalanine	3.5
1.2	Cystine	2.7
1.2	Methionine	3.2
3.0	Threonine	6.7
3.1	Leucine	7.0
1.6	Isoleucine	3.8
2.7	Valine	6.0
6.6	Glutamic Acid	15.0

Both groups also received, daily, 11 mg. of cevitamic acid and one cc. of Betalin Complex (R) intramuscularly. If room temperature and humidity were unusually high, additional quantities of fluid were given to both groups. These groups cannot be compared adequately without consideration for group differences in total calories, carbohydrate, protein and fat; but a relative comparison can be made.

The following procedures were routinely carried out before narcosis, on the third day of narcosis, weekly during narcosis, and three days after termination of narcosis:

1. Glucose tolerance test. Fifty cc. of a fifty per cent glucose solution were administered intravenously to each patient. For a period of at least eight hours before injection, the patients were not given any feedings or nutrient infusions. Blood specimens were collected fifteen, thirty, sixty, and one hundred twenty minutes after the injection. This procedure was omitted with some patients because of their inaccessible veins. Determinations of blood sugar were done by means of the Fiorentino and Giannettasio modification of the Folin Wu Method (5).
2. Serum protein levels, Howe (6) and Kingsley (7) techniques.
3. Serum cholesterol, Bloor's (8) technique.
4. Nonprotein nitrogen, Folin and Wu (9) technique.
5. Calcium, Roe and Kahn (10) technique, modified.
6. Phosphorus, Fiske and Subbarow (11) technique.
7. Serum chlorides, Sendroy (12) technique.
8. Bilirubin, Malloy and Evelyn (13).
9. Cephalin flocculation, Hanger (14) technique.
10. Urine sugar and albumin.
11. Hemoglobin determination and erythrocyte count.

Each patient's weight was recorded prior to and at the conclusion of the experiment.

FINDINGS

All of the twenty-six patients studied lost weight with the exception of one who gained three pounds. The weight loss varied from 0.25 pounds (0.2%) to 19.5 pounds (17.9%), an average of 10.1 pounds (8%). The gavage fed group lost an average of 8.7%, the parenterally fed group lost 7.2%. These results suggest that the quality and/or quantity of nutritional elements absorbed and utilized was essentially the same.

Several causes may be responsible for the weight loss. With the nutritional regime established for these patients, inadequate caloric intake must be con-

sidered, and probably is the greatest factor. According to Elman (3), 1600 calories is the bare minimum required for an average sized adult; our caloric intake was deficient. This was especially true in the parenterally fed group since no calories could be acquired from fat. We were not too much concerned about weight loss as long as protein intake was adequate. A significant factor in the decrease of body mass is the atrophy of musculature resulting from prolonged inactivity. Dehydration must be considered as a possible additional factor, however, it probably did not reach significant proportions.

Protein metabolism in both the patient groups who received feedings by gavage and those who had infusions of protein hydrolysate and glucose preparations compare favorably. Those fed by gavage received 47.5 Gm. and those fed parenterally received 100 Gm. daily. In reviewing the findings, the lower limit of normal total serum protein was arbitrarily set at six grams. Ten different patients had levels below the arbitrary normal on one or more occasions during treatment. One had low levels on two occasions, and one on three different determinations. There was only one patient with a low protein level at the end of treatment. The transient hypoproteinemia is possibly a part of a general protein deficiency as noted by Elman (4), who stated that for every gram of plasma protein lost, 30 Gm. of tissue protein is lost.

For serum albumin, a figure of 3.5 Gm. per 100 cc. of serum was arbitrarily selected as a significant low. Levels below our arbitrary minimum were found in ten patients, in all but three of whom levels rose to normal by the post-narcosis determination. In one case the fall did not appear until after narcosis was terminated. Dehydration may have been a factor in maintaining total protein and albumen levels but attempts to combat dehydration were made by increasing the fluid intake as deemed advisable.

The significant high level for globulin was set at 3.0 Gm./100 cc. of serum. Levels exceeding this occurred in nine patients. Seven elevations were first evident in the post-treatment period, and the others appeared on various days during the period of treatment. This transient elevation in globulin fraction is possibly masking the hypoproteinemia due to a fall in the albumen fraction as indicated by Elman (2). The abnormal findings of hypoproteinemia, albumen depletion, and hyperglobulinemia were distributed as follows:

	Gavage	Parenteral
Hypoproteinemia	4	6
Hypoalbumenemia	7	3
Hyperglobulinemia	3	6

No evidence of nutritional edema was noted that would suggest advanced protein deficiency although Elman (4) found that a critical level of serum albumen able to produce nutritional edema is of little importance because of the great individual variations.

These findings suggest that protein levels were probably adequately maintained by the gavage and parenteral methods, and the protein provided in the hydrolysate was adequate, comparing favorably with that in the gavage mixture. Since twice as much protein was given parenterally as by gavage, more definite comparison is difficult to establish. These re-

sults do not exactly parallel those of a group of Russian workers (15) who found a drop in total protein with a tendency to reversal of albumin-globulin ratio. Lofvendahl (16) likewise reports protein loss in prolonged narcosis.

Fasting blood sugars were performed on all but one patient. Intravenous glucose tolerance tests were performed on most of them (twenty-two) before, during, and after narcosis to determine whether or not any carbohydrate imbalance occurred.

Twelve patients (46%) had a fasting blood sugar elevated over 125 mg./100 cc. at some time during treatment. Two were found pre-treatment, seven on the third to fifth days, and three additional developed elevated sugars during narcosis. Four, one of which had been high pre- and during, were elevated post-therapy. Of the glucose tolerance tests, those with sugar levels above 125 mg./100 cc. at the end of two hours were considered abnormal in this series. Seven were elevated pre-therapy; ten on the third day. Of these, four had been elevated pre-narcosis. Three were elevated at the end of two weeks; two of which had been high previously. After therapy, eleven were elevated; all but one having been elevated at some time previously.

Seventeen cases in all showed elevated glucose tolerance curves at some time, which is consistent with the findings on patients in anesthesia and narcosis (17). Since some of the patients had not been eating adequate diets pre-narcosis and during narcosis and carbohydrate intake was 105.5 Gm. for gavage and 140 Gm. for parenteral feedings, instances of elevated glucose tolerance curves may be expected. Conn (18) and others (19) have demonstrated that abnormal curves will occur if insufficient carbohydrate has been consumed during the period prior to the test.

A breakdown of cases showing abnormal sugar metabolism revealed only slight difference in the incidence of abnormalities. The gavage fed numbered eight, while there were nine of the parenterally fed patients.

Mild to moderate glycosuria appeared at some time during narcosis in slightly more than half of the patients. Twelve were free of glycosuria throughout. Fourteen had definite glycosuria at some time (trace to + plus). One first appeared pre-narcosis, five during the first week, four during the second week, one in the third week, and three post-narcosis.

Of the fourteen cases with glycosuria, eight showed abnormalities in the glucose levels and tolerance tests at periods in narcosis during which glycosuria appeared. In five of the remaining six cases there was an abnormal glucose tolerance test result at some time during narcosis. The sixth case did not have glucose tolerance determinations. These results indicate that the glycosuria probably is due to elevated blood sugar levels in narcosis.

It is evident that narcosis therapy may be accompanied by alteration in carbohydrate metabolism. Mild disturbances of this type have been noted by Horsley (20) in 75% of his cases, most of which were neither maintained at as deep a level nor as long a time as were these patients. Glycosuria, in his experience as in ours, was usually transient. Russian workers (15) failed to find alterations in blood sugar levels in pa-

tients narcotized with Cloetta's mixture. Interestingly enough, studies in anesthesia with morphine, ether, or chloroform reduced the utilization of sugar by the brain in experiments with dogs (21). Anoxia may be the basis for this in our cases as well as in the experimental animals.

Cholesterol levels below 150 mg./100 cc. were rated as low, while findings over 250 mg./100 cc. were described as high. The distribution follows:

Cholesterol	Parenteral Fed	Gavage Fed
Less than 150 mg./100 cc.	6	3
More than 250 mg./100 cc.	1	4

Since the gavage fed patients had a definite high fat intake while the parenteral feedings were fat free, it is significant that the low cholesterol levels occur principally in the parenterally fed patients while the high levels favored the gavage patients. This appears to indicate that it may be possible to vary the cholesterol level by diet since only one case in the parenteral group developed high cholesterol while four in the gavage group did. Not one case from the gavage group had a low cholesterol level post-narcosis. But in the parenteral group, six patients developed low cholesterol and one continued to manifest this level at the routine post-narcosis study.

In all but one case, nonprotein nitrogen determinations were done routinely. Blood urea nitrogen determinations were also done in most of these; their levels closely followed those of the former. An N.P.N. of over thirty-five mg./100 cc. was considered elevated. Only nine cases were completely free of elevations; the remainder showed transient or prolonged increases. Only two of the seven cases of elevated pre-narcosis were high post-therapy. Elevations were noted on the respective days as follows:

3rd day	8 cases
7th day	8 cases
10th day	7 cases
14th day	7 cases
17th day	2 cases
21st day	3 cases

Eight cases were consistently elevated throughout treatment, which varied in duration between four and twenty-three days. Nine cases showed elevated N.P.N.'s post-therapy. The abnormal findings were slightly more frequent in the parenterally fed groups. These findings are contrary to those of a Scandinavian worker (16) who noted decreases in N.P.N. levels following sleep treatment.

Periodic incidences of albuminuria were noted in about half the cases — thirteen normal throughout, one not done, twelve abnormal. Only two were present pre-narcosis, and one disappeared almost immediately. Five cases of albuminuria developed during the first week, five during the second, and two appeared for the first time post-narcosis. By the end of narcosis, the urine of seventeen patients was free of albumin; eight in whose urine there had been albumin. Of the twelve cases which developed albuminuria during or post-narcosis: four were gavage fed, eight were parenterally fed. Whether or not this difference is significant or related to the different type of protein ingested is not clear. These findings support the experience of Horsley (20) who found transient albuminuria in 30% of his cases.

Nineteen patients had cephalin-flocculation tests performed. In eight cases, readings of 3 or 4 plus occurred at some time. One patient was 4 plus pre-narcosis. One and two plus were considered not significant. Abnormalities on various dates with group distribution are as follows:

Day	Number Positive	Gavage	Parenteral
Pre	1	0	1
3	4	1	3
7	2	1	1
10	2	1	1
14	1	0	1
17	1	0	1
21	0	0	0
Post	4	0	4

The cephalin flocculation test results suggest that in many patients a transient impairment in liver function which appeared to correct itself occurred. The incidence of positive tests is much more frequent in the parenteral group. The gavage feeding apparently afforded more reliable liver protection, which is of interest since the daily protein supply in this regimen was not quite half as great as that in the parenteral regime. However, this cannot be definitely concluded since other factors in the parenteral feeding may be involved; as the elevated serum globulin found in the latter group.

Bilirubin determinations were done in four cases, being positive in only one patient, who had hepatitis. Since this test was not made in all the cases in the series; the data we have are not sufficient to suggest any conclusions. Jaundice appeared in one case — apparently due to infectious hepatitis, since the patient had contact with other ward patients who developed hepatitis at about the same time and who were not undergoing narcosis treatment. This was the only case in which direct bilirubin was found. On the basis of the experience of Lofvendahl (16), we should not have expected evidence of jaundice, since in sixteen patients he noted a considerable lowering of the icteric index in comparing pre- and post-narcosis determinations.

The hemoglobin determinations, which were closely paralleled by the erythrocyte counts, were normal in twelve of the twenty-six narcosis. The initial appearance of low hemoglobin in the other fourteen cases occurred at the following times: pre-narcosis 7, first week 2, second week 3, post-narcosis 2.

Hence, seven cases of anemia (hemoglobin under 12 Gm.) developed during or immediately following narcosis. Of these, three were gavage fed, four parenterally. At the close of narcosis there were anemias in ten patients, six of whom had been anemic pre-narcosis.

Chloride fluctuations were present in nine narcosis. Elevations above 600 mg./100 cc. occurred in two cases, while depressions below 550 mg./100 cc. were present in seven cases. Of the two cases with elevations, one was elevated pre-narcosis and fell to normal during narcosis. The other was high on the third day and fell quickly to normal thereafter. One of the seven cases of chloride depression was reduced pre-narcosis and rose to normal by the end of the first week. Three showed transient reduction in the second week but returned to normal, and in three, the

drop manifested itself for the first time after termination of narcosis.

Chloride excretion studies were not done. The factors of fever and loss of chloride through perspiration are probably of very great importance since, in the six cases that developed hypochloremia during narcosis, three had pneumonia prior to its appearance and two had fever over 101.6° F. Another worker who reported a drop in serum chloride is Lofvendahl (16) who further noted no change in sodium. The sodium ion was not studied in our investigation.

Eighteen patients showed, at one time or another, alterations in the levels of calcium, phosphorus, or both. Calcium under 8 mg/100 cc. and phosphorus over 4 mg/100 cc. were regarded as abnormal. Seven patients manifested abnormal calcium, eleven abnormal phosphorus, and four of the two groups combined had abnormalities in both. Of the calcium deficits, two were present pre-narcosis and rose to normal by the first or second week of sleep. Four cases showed isolated findings of low calcium during narcosis with normal subsequent determinations, and one case was low in calcium post-narcosis. Hennelly (22) called attention to a fall in serum calcium encountered in Sonnfaine narcosis.

High phosphorus levels were found pre-narcosis in five cases, all but one of which fell to normal by the first week of sleep. Four cases had isolated readings of high phosphorus at one time during the narcosis. Three were high post-treatment—one of these had been high pre-narcosis.

Of the four cases having abnormalities of both calcium and phosphorus, abnormalities in both elements occurred together on one date in two cases; in others, only one of the elements was abnormal at any one time.

Five of the seven cases with low calcium levels were fed parenterally; two by gavage. Five of the eleven with high phosphorus were fed intravenously; six by tube. Three of the four cases with abnormalities in both elements were nourished intravenously.

SUMMARY AND CONCLUSION

The nutritional aspects of a study of twenty-six patients who were kept continuously asleep for two or three week periods are presented.

Thirteen patients were fed by gavage; thirteen patients by infusions of protein hydrolysate and glucose solutions. Protein, carbohydrate, and fat metabolism, as reflected by plasma and serum levels of the various nutritional substances, were fairly adequately maintained by both the gavage and parenteral methods of feeding.

Chief metabolic alterations consisted in:

1. Transient decrease in serum protein and albumin levels.
2. Disturbed carbohydrate metabolism in slightly more than one half of the cases.
3. Tendency to low cholesterol levels in protein hydrolysate fed patients.
4. Elevated N. P. N. in two thirds.
5. Transient albuminuria in fifty per cent.
6. Positive cephalin-flocculation tests more frequent in the parenteral fed group.
7. Slight tendency for anemia to occur.
8. Hypochloremia in one fourth of the cases.

It appears in the overall picture that the sedation in prolonged narcosis therapy influences metabolic processes, not only of the central nervous system, but also the liver, kidneys, and endocrines.

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THE DETERMINANTS OF THE FOOD INTAKE

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AN UNDERSTANDING of the determinants of the food intake is essential for the rational control of nutrition but considerable confusion has been created by differing definitions or concepts of hunger and appetite, and differing inferences drawn from the food habits of various human groups and the feeding behavior of infants and animals. Distinctions between two types of hunger or two types of appetite were already made before distinctions were made between hunger and appetite. Thus, advocates of the fasting cure, which directly involved the hunger problem, distinguished between normal, natural or instinctive hunger and abnormal, unnatural or habit hunger (1,2). Fletcher (3) distinguished between a normal appetite or desire to eat which indicated nutritional needs and a false appetite or desire to eat which did not indicate nutritional needs. He regarded normal appetite to be of mental origin and to be manifested chiefly by a watering of the mouth for some particular simple food and false appetite to be produced by indigestion or a pre-

vious excessive food intake and to be manifested by general discomfort and stomach craving. Sternberg (4) distinguished between hunger and appetite on the basis of differing connotations of the terms, differences in localization and types of sensations and differences in function. He regarded hunger to be referable to the stomach and to determine the quantitative food intake and appetite to involve smell and taste and to determine the qualitative food intake. However, it remained for Cannon (5) and Carlson (6,7) to place the explanation of hunger on an objective basis by their finding that the pangs of hunger which were referred to in stories of starvation and the common reference of hunger to the stomach were due to sensations produced by periodic contractions of the fasting stomach. The desire to eat in the absence of the pangs of hunger or stomach hunger was attributed to appetite involving taste-memory. Thus a distinction between hunger as the unlearned determinant of the food intake and appetite as the determinant based on learning was incidentally made and this became the main basis of distinguishing between hunger and appetite which was adopted by Ivy (8) and others.

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As a result of the distinction between hunger and appetite which Carlson and Cannon made, I also adopted the view in 1916 that the term "hunger" should be applied to the unlearned determinant of the food intake and "appetite" to the learned determinant but, as indicated in previous papers (9,10,11), I accepted Fletcher's explanation of the determinants of the food intake in 1908 and my impression in 1916 was that the desire to eat which Carlson and Cannon regarded as hunger was merely the desire to eat which Fletcher designated as false appetite. As I found that this desire to eat could be dispelled by ingesting non-nutritive materials, I could not regard it to be normal hunger. Normal hunger, in my opinion, was a desire to eat like that which Fletcher designated as normal appetite. Cannon's and Carlson's concept of hunger was apparently based primarily on observations made during only about 24 hours of fasting. Later, Carlson and a student fasted 5 days for the study of hunger (7) but I believed that more prolonged fasting might be needed in some cases to reveal the essential nature of hunger. I had fasted 26 days in 1913 and did not note that the desire to eat after the first few days was specifically referable to the stomach. An increasing inability to think of anything but food or eating seemed to impel me to break the fast. In the hope of helping to settle the question concerning the nature of hunger, I therefore fasted 15 days in 1917 for a study by Dr. Carlson (12) but it was found that the periodic gastric contractions were manifested throughout the 15 days of fasting and that the desire to eat, although modified after the first few days, was always keenest when the contractions occurred. However, I made daily observations concerning my desire to eat under a variety of conditions during eight additional weeks in 1917 and I was not convinced that the desire to eat associated with the periodic fasting gastric contractions could be regarded as normal hunger (13). The intensity of the desire to eat or need of food associated with the gastric contractions varied and the local sensations which were obviously produced by the contractions often seemed to be distinctly abnormal. Observations made on the contents of the fasting stomach also indicated that variations in bile contamination coincided with some differences in general sensations. At the close of the study, I suggested that hunger might be better explained as a complex of specific hungers but this idea was involved in Fletcher's explanation of normal appetite and led me to try to determine how specific food components were craved already in 1908 (9). I was nevertheless convinced in 1917 that any further explanation of hunger would have to take the findings of Carlson and Cannon into consideration and that the desire to eat associated with the periodic fasting gastric contractions was not a false desire to eat but bore some relation to normal nutritional needs.

Between 1917 and 1923, military service and the manufacture of dietetic cellulose (10) kept me from giving the study of hunger as close attention as it apparently needed to discover anything of further significance but in 1923 I disposed of my manufacturing interests and gave practically all of my attention to the study of hunger and the effect of intermittent fasting and nutrition on general well-being. Thus I found that fasting every other day during over three months became complicated by the development of

nutritional edema. On the days between fasting, I ate as much protein (meat) as I could appreciate but I thought that I evidently ate enough carbohydrate food in addition to the meat to explain the development of the edema. Hence I decided to try a more nearly exclusive carnivorous diet with intermittent fasting. In connection with this, it seemed worth having basal metabolism determinations made at the university as it was expected that the basal metabolism would be increased by the intermittent fasting if the development of edema could be prevented. Dr. Kunde, who previously made a study of the effect of fasting on basal metabolism (14) thought that it would be better to determine first the effect of an exclusive carnivorous and high protein diet without fasting on basal metabolism. Accordingly, after a control period in which a mixed diet was used daily, I abruptly changed to the use of a carnivorous diet daily during five weeks. This diet included beef, veal and pork roasts, glandular organs, blood, rabbits, fowl and fish but no eggs or dairy products. Although I ate as much meat as I could appreciate or tolerate and a wide variety, I felt "starved," particularly during the first few days. In short, in some respects, I felt as I did during the first few days of prolonged fasts. This made it obvious that the discomfort which is generally experienced during the first few days of starvation and which is usually attributed to hunger is mainly due to carbohydrate starvation or due to a change from living on a mixed or high carbohydrate diet to living on an exclusive carnivorous diet (one's own flesh). After the first few days, the "starved" feeling decreased — evidently because I became more or less adapted to the carnivorous regimen. Similarly, the acute discomfort experienced during the first few days of a prolonged fast evidently decreases because one becomes somewhat adapted to living on one's own flesh and some of the sensations commonly attributed to hunger decrease or disappear. Thus, Cannon (15) maintained that hunger disappears after a few days of starvation but his view was based on his preference of the reports of political hunger-strikers to Carlson's and my observations. Advocates of the fasting cure also have claimed that hunger usually disappears after a few days of fasting but they maintained that the hunger which disappears is abnormal, unnatural or habit hunger and that normal, natural or instinctive hunger develops when health has been restored by nature while fasting.

Further evidence that the acute discomfort or "hunger" which is commonly experienced while fasting only one or two days is mainly due to a lack of adaptation to a carnivorous diet or to living on one's own flesh was obtained during the second five weeks of my trial of the exclusive carnivorous diet. I then fasted two successive days each week. On the first of these two-day fasts, I usually felt better than on the days when I ate as much meat as I could appreciate. No discomfort was produced by the transition from living on the carnivorous diet to living on my own flesh. Evidently I even felt better on the first day of these fasts than when I ate because more fat or a more physiologic proportion of fat was utilized when I fasted than I used when I ate. That is, when the trial of the carnivorous diet was planned, the intention was to use mainly lean meat but, like Stefansson (16), I

found that a liberal proportion of fat is needed to make it possible to tolerate a carnivorous diet. Pork and eel tasted best but a craving for some carbohydrate food developed and I yielded to this after 10 weeks.

Although the acute general discomfort and the sensations produced by the periodic gastric contractions during the first few days of fasting following the use of a mixed or high carbohydrate diet decrease with more prolonged fasting, I never found the desire to eat to disappear in eight fasts of eight to 41 days. After about the sixth day of fasting, it always became increasingly difficult to resist a practically continuous desire to resume eating. It seemed that it would have been possible to ignore the desire to eat associated with the periodic gastric contractions if more or less complete relief had been obtained between the periods of gastric contractions. The increasing interest in resuming eating was associated with an increasing appreciation of the aroma of, or a specific craving of, protein foods. Glaze (17) noted that roast beef appealed most to him toward the end of 17 days of fasting. Ham appealed most to me in my 33- and 41-day fasts in 1925. Fruit hardly made a greater appeal than flowers as food although I usually broke prolonged fasts with some fruit juice to satisfy myself that my stomach was still able to retain food. Food seems to have a deeper meaning after more or less prolonged fasting. It more clearly appears to contain life — life that one can consume and make part of one's own life.

Early in 1924 or shortly after my 10-week trial of the exclusive carnivorous diet, I obtained clear evidence in an unforeseen way that the periodic fasting gastric contractions could occur without giving rise to any desire to eat and that the experience of a desire to eat with the contractions depends on the need of some food. Similarly, the desire to eat experienced between the periodic fasting contractions or with the stomach more or less full of food is evidently always due to some need of food. My observations in 1917 left the question open whether the periodic fasting contractions increased the desire to eat directly or whether they merely increased the awareness of the desire to eat by adding the epigastric sensations to an already existing desire to eat. Carlson believed that the gastric contractions gave rise to the desire to eat (hunger) directly because he was able to induce gastric contractions and the associated sensations in his gastric fistula subject but Carlson and Cannon never ruled out the existence of the desire to eat which they attributed to appetite when the desire to eat which they regarded as hunger was manifested. I found no clear evidence before 1924 that the periodic fasting gastric contractions could occur without giving rise to a desire to eat but this became evident as a result of a change in my eating habits which was made to determine whether sleeping with the stomach empty would be of special benefit.

The idea that sleeping with the stomach empty might be of special benefit was suggested by the practice of Sanford Bennett, "The man who became young at 70" (18). G. Stanley Hall, who investigated claims of rejuvenation (19), was of the opinion that Bennett's claim was justified. Bennett stated that he ate like a boy but always emptied his stomach before he

retired. It seemed to me that emptying his stomach before he retired was the only unusual thing that he did but I thought that it would be better to try eating food early enough in the day so that my stomach would naturally become empty before I retired. During the preceding 16 years I ate most of my food relatively late in the day. First, I adopted the no-breakfast plan advocated originally by Dewey and popularized by Fletcher. Later, I tried eating only in the evening. Thus my stomach was often overloaded when I retired and my sleep was disturbed. Usually I did not even care for food early in the day and I therefore began changing my habitual time of eating by first reducing my food intake one evening so that I would become likely to appreciate food earlier than usual on the next day.

Before noon on the next day, I ate about as much food as I could appreciate. My stomach felt considerably distended but I was not entirely satisfied. During the afternoon I permitted myself only sweetened drinks. The gastric distention gradually decreased and at the same time the desire for more food or sweetened drinks decreased. Nevertheless I expected to have some difficulty with my habitual desire to eat in the evening. In fact I expected it to take a few weeks and possibly months before I would become satisfied with eating mainly early in the day. However, my stomach became empty early in the evening and periodic gastric contractions developed but I had no desire to eat whatever. A bar of almond milk chocolate within arm's reach while the "hunger contractions" were in progress made no more appeal to me as food than a stick of wood might have made. I never felt more completely satisfied in 10 years. Before this, I often thought that the best time to do mental work would be at such a time when there is no distraction by thoughts of food or eating but I found that this was apparently the best time to fall asleep. I woke the next morning when a period of fasting gastric contractions was evidently in progress and this was accompanied by a slight desire to eat.

These and subsequent observations made it obvious that the periodic fasting gastric contractions do not give rise to a desire to eat unless some need of food exists. Carlson previously found that the first or first few periods of hunger contractions following a meal did not give rise to as keen a desire to eat as later periods. My early eating regimen merely made the contrasts more extreme. It also became clear that true satiety is not produced by simply filling the stomach with food. This produces epigastric ease or a fullness which apparently only inhibits the desire to eat. If the nutritional needs are not excessive, gastric fullness is likely to be replaced by complete satiety without the ingestion of more food but, if the needs are considerable, as after food restriction or fasting, a desire for more food is likely to persist even when the stomach is disagreeably distended with food. If one continues eating until one is completely satisfied, a large part of the food in the digestive tract is likely to represent an excessive intake.

Thus, what seemed to have been a personal hunger problem during the preceding 16 years was incidentally solved. In the study made in 1917, it was found that I needed more food than enough for maintenance to barely satisfy my desire to eat. Dr. Carlson regarded

this as evidence of bulimia but it became clear in 1924 that this "bulimia" was simply due to the keen desire to eat of apparently central origin created by the restriction of my food intake early in the day and my attempt to dispel this desire to eat rapidly and completely late in the day by eating enough food. However, I have had no difficulty during the 26 years that have passed since 1924 in controlling my food intake when I ate daily and I have repeatedly found it possible to reduce my intake somewhat below the maintenance level without experiencing a desire to eat which could not easily be ignored. I have been doing this by simply eating most of my food relatively early in the day or merely by avoiding eating unnecessary food late in the day. It has been of repeated interest to note that, if approximately enough food has been eaten and a moderate desire for more food persists or develops later because of slow digestion or slow absorption, this desire to eat disappears if one only waits until enough of the ingested food is digested and absorbed.

In reporting my findings in 1927 (20), I regarded the desire to eat to be hunger as I always found it to be based on needs. Moreover, the desire to eat which I was particularly interested in explaining was the desire to eat ordinarily associated with the periodic fasting gastric contractions and which Cannon and Carlson regarded as hunger. I did not try to explain appetite but indicated that it could not be distinguished from hunger as a different desire to eat. I was well aware that a learned or conditioned aspect of feeding behavior existed but I believed that this (appetite) could not be explained or clearly distinguished from hunger until the nature of specific hungers (cravings based on needs) was better understood. My failure to explain appetite may explain why Cannon (21) referred to my paper as a "slur" on the distinction between hunger and appetite. He thought that Dr. Carlson should not have permitted the publication of the paper. As Cannon's objection did not appear to be based on any experimental work, I believed that it could be ignored. The validity of my explanations seemed to be self-evident and my experimentation could easily have been repeated by others. However, Cannon's views continued to be widely accepted and additional experimental evidence that the periodic fasting gastric contractions or gastric sensations are not essential in the desire to eat was apparently obtained by others (22) only relatively recently.

Reactions like Cannon's to my findings concerning the nature of hunger and the fact that my personal hunger problem appeared to have been solved led me to give my attention between 1927 and 1942 mainly to other subjects but by 1942 my general desire to eat had distinctly declined and it seemed of interest to determine the extent of the changes that occurred in at least the secretory activity of my fasting stomach since the first observations were made in 1917 and since more observations were made between 1925 and 1929 (23, 24, 25). A considerable decline in my gastric secretory activity was discovered but of more importance was the finding of evidence that interrelations existed between the fasting gastric acidity, gastric motility, nutritional hydration and the appreciation or tolerance of food (9, 26, 27, 28). It

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became clear that dehydration produced some degree of anorexia by decreasing the flow of saliva, the gastric secretion and evidently also other digestive secretions. Dehydration obviously occurred in prolonged fasting and at least partly explained the seeming decrease or disappearance of "hunger." It also explained the failure of a normal appetite, such as Fletcher described, to develop by simply waiting for it to develop. That is, I began restricting my food intake greatly or first tried to fast in 1908 to restore a normal appetite. I evidently lost my appetite before that by already restricting my food intake too much in connection with training for long distance running and other physical activities. My object was merely to keep my weight down but prolonged moderate restriction of my food intake, the use of a diet that was somewhat poor and strenuous exercise evidently led to dehydration with reduced digestive secretions and the development of digestive disturbances with a lack or loss of appetite. Fletcher's claim that a normal appetite could be restored by simply waiting for it to develop seemed logical to me in 1908 and it was 1942 before it became clear why this could not occur in a nutritional state involving dehydration. The importance of normal hydration as a basis for the manifestation of a normal appetite became obscured early in my experience by the development of obvious nutritional edema.

As already implied, I regarded the decrease in the appreciation of food with dehydration in 1942 to be a decrease in appetite rather than in hunger. Carlson (7, 12) realized that the desire to eat after the first few days of starvation was somewhat obscured by an impairment of appetite but he and Cannon did not distinguish between the appreciation of food and the desire to eat associated with appetite just as they did not distinguish between the sensations produced by the periodic fasting gastric contractions and the desire to eat associated with these sensations. The existence of a difference between the appreciation of food and the desire to eat is not obvious because some desire to eat always exists when food is appreciated but a distinction can be clearly conceived if appetite is more broadly regarded as determining the choice, acceptance, appreciation or rejection of specific foods. Obviously a desire to eat (hunger) can exist without the appreciation of food (appetite) when the available food is rejected. There is no evidence of more than one desire or drive to eat and the appreciation of food is clearly determined by some factors that are not essential to a desire to eat. The desire to eat (hunger) is determined by internal or central conditions or needs and can be experienced without contact with food. The appreciation of food (appetite) depends on the nature of the food as well as on needs and concerns mainly peripheral reactions, such as mouth-watering and gastric juice secretion, to actual or imagined (learned) contact with foods. The relative unimportance of taste-memory in appetite is indicated in a state of complete satiety.

Since I made the foregoing type of distinction between appetite and hunger (9), Ivy and his associates or students published papers (8, 22, 29, 30, 31) in which they stress central factors in hunger as I did but in which they still follow Cannon and Carlson in distinguishing between hunger as the unlearned ele-

ment in feeding behavior and appetite as simply the learned element. Like Cannon and Carlson, they also fail to distinguish between the desire to eat and the appreciation of food. Moreover, they (31) do not regard hunger to involve a desire to eat but maintain that the desire to eat is learned (appetite). Their explanations of hunger and appetite support the use of amphetamine as an aid in weight reduction but otherwise their explanations seem to be of no value for the practical control of the food intake.

The distinction between hunger and appetite which Janowitz and Grossman (31) in particular explain involves the nature-nurture controversy. In my opinion, we become instinctively aware of the desire to eat when we reach the necessary stage of physical, including neural or cerebral, development and we learn what sensations we commonly experience when we have a desire to eat. Evidently the newborn infant is not aware of a desire to eat or to suckle but the infant is an underdeveloped organism normally dependent on the awareness of its mother for the ingestion of food. However, very young children seem to know with certainty when they desire to eat or are hungry but they and even many adults are likely to be perplexed or vague concerning the bodily sensations that they experience when they desire to eat. Even Cannon did not learn with certainty that the pangs of hunger were of gastric origin until this was revealed by the experience of his student, Washburn. Individuals who question the existence of a relation between the desire to eat and the stomach usually become convinced by a personal experience with the balloon method of study which makes the local sensations clearer. Vagueness and erroneous learning evidently partly explain the reference of the desire to eat to different bodily sensations by different individuals. Obviously needs are not periodic like the sensations produced by the periodic fasting gastric contractions but nutritional needs are even less likely to be directly related to the feeling of generalized weakness, fatigue, dizziness, headache and other "hunger sensations" to which Janowitz and Grossman refer. Nevertheless there is no doubt that many individuals with only a vague desire to eat, eat to dispel a feeling of weakness, fatigue, headache or the like. Gastric pangs certainly can be dispelled by the ingestion of food but only a small amount is needed for this and the persistence of the desire to eat after that remains to be explained. The existence of a central drive which persists until inhibited by gastric fullness or satisfied by the absorption of enough digested food provides a more adequate explanation of feeding behavior. However, the desire to eat would still be based on needs if it were learned, as Janowitz and Grossman maintain, from starvation sensations but the justification of regarding the desire to eat to be learned if it invariably arises from conditions in the organism may be questioned.

The explanation of human feeding behavior is complicated by infantile and childish stages as well as by the feeding behavior of people who never grow up. An example of mammalian behavior which is not complicated by immature stages is maternal behavior such as can be observed in the rat. I have made observations on rats in connection with the production of over 2500 litters including about 1000 first litters.

Not infrequently as many as 10 to 15 young are produced in a first litter and the mother usually acts as if she knew exactly what to do. The mother is likely to remove (eat) all of the placentas and umbilical cords systematically and otherwise properly care for the young. The mother is evidently aware of what she is doing and presumably desires to do what she does but, like many humans, she probably has no rational idea of what she is doing or why she desires to do what she does. Innate mechanisms, hormones and a complex neural development evidently explain this unlearned behavior but rats also vary in their maternal efficiency. Occasionally a mother not only removes the placentas and cords but bites off the tails of some of the young and does this with successive litters. More rarely, a mother bites off one or more legs of the young but otherwise takes normal care of them. Apparently such mothers are unable to distinguish clearly between appendages that should be removed (placentas and cords) and appendages that should not be removed (tails and legs). The cannibalism of some mother rats is probably also due to the inheritance or development of an inadequate maternal I.Q. For biological survival, adequate feeding behavior is at least as important as adequate maternal behavior and this suggests that feeding behavior or the nutritional I.Q. is also largely determined by inherent mechanisms. Dove's study (32) likewise indicated this. Learning is evidently a greater factor in mature human feeding behavior than in that of lower animals but learning appears to be a superficial factor and learning thus far does not seem to have resulted in a better adjustment of the human food intake to needs.

A conditioned aspect of feeding behavior nevertheless exists which is produced by the food that is customarily eaten. Thus, Stefansson (16) found that some dogs, especially old females, raised on caribou meat, would almost starve to death before they would eat seal meat — and vice versa. I have also noted that some rats raised on a relatively poor diet hesitate a great deal before they will eat freely a better diet and one that they prefer later. I had such conditioning in mind when I previously (9) distinguished between an acquired or conditioned appetite and a basal or physiologically determined appetite. The inability to appreciate a specific food or diet may often merely be due to a lack of adaptation to its use but the nature of such adaptation remains to be clarified and my experiences again suggest that innate or constitutional factors are the most important determinants of the ability to "learn to like" specific foods. I was never able to "learn to like" onions although other members of the family liked them and I made some deliberate attempts to overcome my dislike or intolerance of them but I deliberately "learned" to prefer a high fat diet to a high carbohydrate diet. Adaptation which is not spontaneous or inherent evidently involves physical changes which become the basis of subsequent appreciation and which tend to become permanent changes or harder to modify with aging. However, the making of changes in acquired food habits can apparently be facilitated by more or less prolonged fasting. This evidently serves to restore a basal appetite.

In discussing the relation between appetite and nutritional needs, Janowitz and Grossman refer to

studies on infants and animals which indicate that appetite may or may not reflect needs. However, tests on infants and animals do not reveal why specific foods are selected or rejected except by inference. Observations concerning my own appetite indicated that a keen appreciation of specific foods was always based on needs but some needs, like the need of a relatively high proportion of fat in a carnivorous diet, are specifically gastro-intestinal needs. During 20 years in which I lived alone and often tried unusual diets, I was repeatedly impressed by the fact that appetite generally was a more reliable guide in nutrition than presumed knowledge. Incidentally, my study of the nature of "protein hunger" (9, 24, 25) revealed that the depletion of a specific nutrient does not necessarily produce conditions in which the deficient nutrient is particularly appreciated. That is, protein restriction was found to increase the gastric acidity and give rise to a desire to eat associated with far more imperative epigastric "hunger" or pain sensations than those produced by the periodic fasting gastric contractions under ordinary conditions but protein (lean meat) was not appreciated. Evidently it could not be appreciated because it further stimulated the acid gastric secretion which gave rise to the disagreeable "protein hunger sensations." A high proportion of fat rather than protein was needed to reduce the gastric acidity and promote epigastric comfort, although some protein was also needed to reduce the hyperacidity more permanently. The fat represented a gastro-intestinal need; the protein a general or central need. In short, pathological situations are likely to be produced when such experimentation is carried to extremes. In rats and mice, pylorospasm, gastric retention and peptic ulcers, including perforated ulcers, were produced by protein starvation (33, 34).

Under less extreme conditions, I found that appetite clearly indicated the need of protein, some carbohydrate food, vitamin A and apparently some other (unidentified) vitamins and salts. "Vitamin A hunger" was experienced before I knew that there were fat-soluble vitamins or that ice-cream and butter contained any vitamin. I made repeated attempts to ignore or discourage my cravings for ice-cream or butter during a period in which I believed that a fruit and nut or monkey diet was the ideal diet for man but I eventually decided to include some cream and eggs in my diet to supply the apparent vitamin-like substance which ice-cream and butter seemed to supply. Later, when I began using liberal amounts of meat in my diet, I used ice-cream daily to satisfy my cravings but, after learning that bone marrow as well as ice-cream, butter, cream and eggs supplied vitamin A, I began using bone marrow in my diet. As a result, I completely lost my appreciation of ice-cream. It may be that I incidentally obtained some needed calcium from the bones which contained the marrow. Appetite may only serve to prevent a serious deficiency of some essential food components and it may serve well in the selection of an adequate diet only from more or less natural foods. Obviously appetite must be relatively keen to serve well in the selection of food and appetite is not merely taste (9).

In my opinion, the further explanation of the determinants of the food intake will largely depend on observations made by investigators primarily on themselves. Studies made on others or on animals are of value in testing the results of personal experience but they are not an adequate substitute for the personal experience of hunger and appetite. Although individuals differ in some respects, it is not likely that the essential determinants of the food intake differ significantly in individuals that are not obviously abnormal. One source of confusion in the past seems to have been the attempt to explain feeding behavior completely and clearly on the basis of only two major determinants — hunger and appetite. In 1944, I (9) distinguished between a basal appetite and an acquired appetite. Since then, it occurred to me that the explanation of feeding behaviour would be facilitated by also distinguishing between central hunger and gastro-intestinal hunger (central hunger with gastro-intestinal components). The periodic fasting gastric contractions do not give rise to a desire to eat when there is no need of food but there still is no proof that they do not directly increase the desire to eat when a need of food exists. This seems more certain when the influence of the gastric secretion and the relation between gastric acidity and motility is considered. The need of food, particularly protein, increases the fasting gastric acidity and gastric tension or tonus and this may serve as part of a feedback mechanism to increase the desire to eat until the feed-back is interrupted by the ingestion of sufficient food. Moreover, in desiring to eat, we evidently mean that we desire to reduce some epigastric tension or to stop the digestive tract from irritating or digesting itself. The recognition of four major determinants of the food intake instead of the conventional two determinants also only represents a further factoring which began when it was realized that the food intake is determined by more than one factor—simple hunger or simple appetite. Obviously there are many minor factors.

SUMMARY

An analysis of the determinants of the food intake is made on the basis of the personal experience of the author in attempting to control his own food intake. Hunger and appetite are distinguished as factors serving different functions in the food intake. Hunger is regarded as the desire to eat which impels one to seek food, try things as food or continue eating accepted foods until the desire to eat is inhibited or satisfied. Appetite is regarded as the factor that determines the acceptance (appreciation or rejection) of specific foods. Hunger was found to be of apparent central origin and based on needs but also influenced considerably by gastro-intestinal conditions. Hence it is suggested that a distinction be made between central hunger and gastro-intestinal hunger. Appetite is regarded as involving chiefly peripheral reactions, such as mouth-watering, to actual or imagined (learned) contact with foods and a distinction is made between a basal appetite determined by needs and an acquired appetite conditioned by the nature of some foods. The importance of innate factors rather than learning as determinants of the food intake is emphasized.

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ABSTRACTS ON NUTRITION

HOLT, J. F.: *Vitamin D resistant rickets (refractory rickets)*. *Am. J. Roentg. & Rad. Ther.*, 64, 4, Oct. 1950, 590-602.

Refractory rickets is a peculiar, apparently hereditary form of late rickets not associated with recognizable visceral disease, and characterized by dwarfism, severe deformities, persistent hypophosphatemia and good therapeutic response to very large doses of vitamin D. Diagnosis depends on finding unequivocal signs by x-ray and the following conditions must be differentiated — chondrodystrophy, osteogenesis imperfecta, hyperparathyroidism, renal rickets, the de Toni-Fanconi syndrome, and late privational rickets. Once the diagnosis is made, the necessary, tremendous doses of vitamin D are begun (sometimes as much as 100,000 units or even 500,000 units daily) and the patient carefully watched for the development of signs of vitamin D intoxication.

FYER, C. C. F.: *Hemoglobin determinations of 1265 Bunbury school children and of a small group of adults*. *Med. J. Australia*, Sept. 30, 1950, 508-512.

Because of the reports of a high incidence of anemia in the south west of Western Australia the authors undertook a hemoglobin survey among school children in that area. Most of the paper deals with the technique employed in making the readings. She used an "Eel" photoelectric colorimeter for measuring the color density of solutions of alkaline hematin, employing an inorganic standard originally described by Gibson and Harrison (*Biochemical Journal*, 1945, vol. 39, p. 490). The mean hemoglobin levels were as follows: 1265 children aged 5 to 16 years, 14.1 gm. per cent. 1049 children aged 5 to 13 years, 14.0 gm. per cent. 68 adults were examined and the mean value for males was 15.9 gm. per cent, and for females, 14.3 gm. per cent. These

values are considered satisfactory and in agreement with most recently accepted standards of normality in Great Britain, viz., 14.8 gm. per cent equals 100 per cent.

SHIPLEY, R. A., STORAASLI, J. P., FRIEDEL, H. L., and POTTS, A. M.: *¹³¹I in the diagnosis and treatment of hyperthyroidism*. *Am. J. Roentg. & Rad. Ther.*, 64:4, Oct. 1950, 576-589.

Normal subjects retain 45 per cent of the radioiodine given orally in a single dose. The average patient with hyperthyroidism retains 83 per cent of the dose given. In a series of 29 diffuse goiters treated with a mean dose of 95 microcuries of ¹³¹I per gram of thyroid, 78 per cent were controlled, 15 per cent failed to respond to a single dose, and 7 per cent relapsed. Myxedema occurred in 15 per cent. The gland usually returned to normal size. In a group of 18 cases of nodular goiter treated with a mean dose of 135 microcuries per gram, 83 per cent were controlled, 17 per cent failed to respond, and there were no cases of relapse or of myxedema. The gland usually did not return to normal size. The danger of late carcinogenic effects of radioiodine cannot be ruled out until treated patients have been followed for many years.

UNGLEY, C. C.: *Absorption of vitamin B₁₂ in pernicious anemia. I. Oral administration without a source of intrinsic factor*. *B. M. J.*, Oct. 21, 1950, 905-908.

The absorption of vitamin B₁₂ was studied by comparing the effective oral dose with the parenteral dose expected to produce a similar increase of red cells in 15 days. In one case daily doses of 5 megm. gave no response. In another, 80 megm. a day for 24 days produced an increase in red

cells no greater than would have been expected in 15 days from the injection of 2.5 megm. The response to injected material was normal, so that the corrected oral-dose/parental-dose ratio was several hundred to one. By contrast, the oral-dose/parental-dose ratio in 5 cases given a single dose of 3000 megm. by mouth was from 20 to 40:1, the increase in red cells being so great in 15 days as to suggest the absorption of from 80 to 160 megm. or more. Very little of the vitamin can have interacted with Castle's intrinsic factor, because of the low quality and quantity of the gastric secretion in pernicious anemia. Further tests are needed to determine if more vitamin B_{12} is absorbed from a single large dose than from the same quantity of material given in divided daily doses.

UNGLEY, C. C.: *Absorption of vitamin B_{12} in pernicious anemia. II. Oral administration with normal gastric juice.* B. M. J., Oct. 21, 1950, 908-911.

The effect of vitamin B_{12} given with normal gastric juice was observed in 8 patients with pernicious anemia. The total amounts were usually 50 megm. plus 500 cc. given as a single dose or in divided doses.

One patient failed to respond to oral therapy. In one who received 40 megm. with only 150 cc. of gastric juice the response was very poor. In two patients the oral-dose/parental-dose ratio was 10:1, suggesting that about 10 per cent of the vitamin had been absorbed. In the remaining four cases the response was about as good as would have been expected if the same dose of vitamin had been injected. Thus small doses of vitamin B_{12} given with normal gastric juice are sometimes efficiently absorbed. The amount of gastric juice necessary to promote the absorption of a given amount of vitamin varied considerably from patient to patient. These differences may indicate differences in the amount of intrinsic factor in the gastric juice but differences in the recipients may have been equally important.

UNGLEY, C. C. (with the assistance of G. A. CHILDS): *Absorption of vitamin B_{12} in pernicious anemia. III. Failure of fresh milk or concentrated whey to function as Castle's intrinsic factor or to potentiate the action of orally administered vitamin B_{12} .* B. M. J., Oct. 1950, 911-915.

Ungley confirmed the findings of Ternberg and Eskin that normal gastric juice combines with vitamin B_{12} and renders it unavailable to certain bacteria. He sought to determine if milk or concentrated whey might possess similar properties. Neither milk or whey concentrate in the doses employed was an adequate substitute for normal gastric juice as a source of Castle's intrinsic factor. Only very slight responses were obtained, no greater than might have been expected from vitamin B_{12} alone.

UNGLEY, C. C.: *Absorption of vitamin B_{12} in pernicious anemia. IV. Administration into the buccal cavity, into washed segment of intestine, or after partial sterilization of the bowel.* B. M. J., Oct. 21, 1950, 915-919.

Efforts were made to determine whether vitamin B_{12} would be effectively absorbed if the possibly destructive action of intestinal juice could be reduced or avoided. Application of 5 megm. to the buccal mucosa gave a negative response in a patient who subsequently responded to the same quantity of vitamin given with gastric juice. In two patients the instillation of vitamin B_{12} with or without gastric juice into a washed segment of the intestine isolated between the two balloons of a Miller-Abbott tube led to negative or trivial responses. In each case the subsequent administration of

the vitamin by injection or orally with gastric juice was effective.

Even after preliminary partial sterilization of the intestine with aureomycin and other drugs the oral administration of 80 megm. of vitamin B_{12} was ineffective. The patient subsequently responded to the same dose of the vitamin given with gastric juice. The negative findings are against the possibility that Castle's intrinsic factor acts by protecting the vitamin from destruction in the gastro-intestinal tract. They do not, however, entirely exclude such possibility.

PALMER, L. J.: *The application of the insulins in the treatment of diabetes mellitus.* Journal Lancet, LXX, 10, Oct. 1950, 386-388.

Timing of the effects of insulin in treating diabetes is of utmost importance. Some type of slow-acting, long-acting insulin should be employed alone in the maintenance regime and once daily in all diabetics requiring insulin, provided the daily requirement does not exceed 30 units. Protamine zinc insulin now usually is employed. "Old" insulin is best in emergencies. Mixtures of "old" with protamine zinc insulin may be made to suit almost any type of "timing." The new insulin, NPH, a crystalline product of zinc protamine insulin, gives great promise of usefulness, partly because crystalline insulin can be added to it without altering the quick-acting effect of the addition.

MOYER, J. H. AND WOMACK, C. R.: *Glucose tolerance tests (relative validity of four different types of tests).* (Texas State J. M., 46, 10, Oct. 1950, 763-768).

Using 103 normal subjects as controls, the standard oral glucose test showed the two-hour blood sugar level to be highly selective, being both sensitive and specific. The authors considered 120 mg. per 100 cc. or below as normal in the 2-hour sample. This oral glucose "standard" test is the best test available. Estimation of the blood glucose two hours after a meal is a simple presumptive test of carbohydrate metabolism, but lacks the sensitivity of the standard test. The intravenous glucose test is valuable in the presence of gastrointestinal disease. The Extol-Rose, two-dose test is overly sensitive, and should be discarded, since, when used alone, it results in many fallacious diagnoses of diabetes. Fasting blood sugar and a blood sugar two hours after ingesting 100 gms. of glucose gives all the data required and constitutes a simple procedure.

HARGROVE, C. J.: *Retinal changes in diabetes mellitus.* (Texas State J. M., 46, 10, Oct. 1950, 772-774).

In a study of 59 diabetic patients, capillary fragility tests were positive in 19 of the 25 patients investigated, and 44 percent of this group presented characteristic diabetic retinal changes. There appears to be a tendency toward capillary fragility in diabetic patients but there is no correlation between retinal hemorrhage and capillary fragility. Capillary fragility tests are not quantitative and have real limitations. Diabetes appears to be a vascular disease as well as one in which the sugar metabolism is disturbed, and any etiological hypothesis of the disease must include both features.

JOHNSON, A. L., SCOTT, R. B. AND NEWMAN, L. H.: *"Tween 20" and fecal fat in premature infants.* (A. J. Dis. Children, 80, 4, Oct. 1950, 545-550).

The effect of "tween 20", a new wetting agent, on fecal fat was studied in 13 premature infants and in 2 full term infants with steatorrhea. Fecal fat content was analyzed before, during and after the administration of the emulsifier. Six of the 13 premature infants failed to show increase in fat retention during the administration of the drug. Seven of the infants showed a slight increase in fat retention while taking "tween 20." This agent was no more effective in reducing fecal fat than was skim milk alone. "Tween 20" is, however, apparently non-toxic.

JOHNSTON, J. A.: *Factors influencing retention of nitrogen and calcium in period of growth. VIII. Influence of rest and activity.* (Am. J. Dis. Children, 80, 4, Oct. 1950, 551-555).

In children with normal temperature and pulse rate, the retention of nitrogen and calcium is diminished by bed rest and improved with moderate activity. In pulmonary tuberculosis, even when normal temperature and pulse rate obtain, this is not true, due presumably to the necessity of replenishing depleted reserves. Early ambulation ought to be part of the regimen for any chronic illness when the vital signs are normal.

EDITORIAL

THE FOOD-POPULATION PUZZLE

As a world society we must find prompt means of producing food or else resort to some method of limiting population increase. Both measures may need to be employed because at present the food supplies of the world are utterly inadequate to nourish the people who inhabit it. This is possibly the most challenging fact in all history and it has emerged so suddenly that few persons realize its urgent importance. The food barrel is being scientifically scraped and statistics tabulated to discover by what magic global products can be sufficiently augmented. Nutritional scientists are busy on this stupendous food problem now, and many astute physiologists are considering how the population of the Earth can be controlled. The United Nations Educational, Scientific and Cultural Organization, the Food and Agricultural Organization, the U. S. Commission for UNESCO, the FAO Inter-agency Committee of the U. S. Government, the Department of Agriculture and numerous private organizations representing farm, labor, consumer and other interests, as well as our State Department, are most vitally interested in placing this vast problem before the peoples of all nations for serious consideration. For the moment at least, birth control is being played down, in the hope that Food can be brought into balance with People, rather than that People should be forced into balance with Food.

AN OVERCROWDED AND QUARRELSOME SOCIETY

Only one-third of the world's people get enough of the right kind of food and this third consume three-fourths of the world's entire food supply. One-half of the human race today remain constantly in a state of hunger. The specters of famine and starvation haunt society today as diligently as in any period of history. Disease, lowered efficiency and serious tensions in the social, economic and political fields are traceable directly to this master cause. These extreme statements may readily be doubted in so prosperous a nation as ours, but available statistics from many areas fully confirm them.

The difficult problem of food and people obviously is not a novel one, but it has been newly clarified in the global viewpoint forced upon us by the upheavals of the past decade. Isolationism was of necessity replaced by an alert and analytic interest aimed at detecting the basic causes of war and the fundamental conditions favoring peace. One of the seeds of war is hunger. Malnutrition predisposes to unsound judgment and the uncritical reception of propaganda. The former growth of fascism and the present spread of communism have centered around flagrant misrepresentation of economic facts, which no well-fed population would be capable of believing. Since food is wealth and wealth is one objective of most aggressive wars, the belligerent tendency is harder to inculcate in prosperous well-nourished peoples.

Once the vastness of this problem of food scarcity became plain, it was soon recognized to be not a conditioned scarcity due to local factors of production but rather an absolute scarcity, depending more on the factor of population increase than productive failure. As closely as can be determined, there are 2 1/3 billion people in the world today, and the rate of increase is roughly one per cent per year. In the past ten years the human race has added 200 million new members. Every 24 hours a positive balance now occurs between deaths and births of nearly 70,000. Every minute there are 50 more births than deaths. This unprecedented acceleration of population increase is out of all proportion to the increased production of food. The wide-spread dislocations of World War II caused innumerable foci of complete food lack and fatal starvation, in addition to those due to natural and chronic causes.

WHY SOME PEOPLE DO NOT EAT

Food production on a global scale can be appreciably increased, but only through expensive, organized effort over a period of many years. Of the Earth's 36 billion acres of land surface only 3.6 billion acres now are under cultivation, and 18 billion acres can never be tilled. Part of the 90 billion acres of sea area contribute significantly to the

food supply, and will contribute more in the future through far-off-shore fishing. New land potentials of 1.3 billion acres in tropical regions can eventually be opened up to cultivation. Presently tilled areas can be made to yield 20 per cent more produce through the application of scientific knowledge now at our command. Thus there are possibilities of raising the yearly food supply by approximately 40 per cent, but some authorities believe that an increase of food of something like twofold is needed in order adequately to feed humanity. Some advance can be realized by cutting down wastage and loss of food after it has been produced through improved cookery and the extension of efficient refrigeration. One-fifth of the total grain crop is annually destroyed by pests, infestation and disease — an amount sufficient to feed 300 million people. The prevention of soil erosion in the United States alone would save 2 1/2 million acres annually which are now being lost through this factor. Bovine mastitis, which is responsible in Europe for the annual loss of 1500 million gallons of milk, could be almost completely eliminated by treatment with penicillin. Enclosed areas might be fertilized to increase the yield of fish. Food yeast could be grown in immense quantities on culture media derived chiefly from wood and useless plant products.

Only about 10 per cent of food moves in international trade but this 10 per cent is important. Since North America has become the world's largest supplier of agricultural and industrial goods, and since the countries desiring these products have little to offer in exchange for them, a serious bottleneck has developed. It has resulted, for example, in the indefinite continuance of food rationing and price control in Great Britain, and the much-publicized piling up of agricultural goods in dollar countries. This is but one of the world factors which eventually might force the adoption of federation in order to obviate or at least modify the present confusion of currencies and customs.

The world's food poverty must grow worse for a time at least because of the unprecedented acceleration of population growth out of all proportion to the increase of edible products. Estimates by some nutritionists suggest that the earth can be made to feed its increasing population, but many other students of the problem are less optimistic. Cereals must be increased 50 per cent, meat 100 per cent, vegetable oils 125 per cent, milk 150 per cent, and fruit and vegetables no less than 300 per cent. Success depends upon bringing technological knowledge to a large enough sector of the impoverished areas, but this takes time and such knowledge is not too effective without suitable implements and without industries capable of manufacturing them. President Truman's "Point 4" is aimed partly at this very aspect of the problem.

REALISTS AND PURISTS

Since the last World War the United States has contributed vast sums of money to such programs as Marshall Plan aid, the British Loan, Greek-Turkish assistance and a number of international organizations attempting to feed impoverished peoples in war-devastated countries. In the fiscal year 1949 no less than \$6.5 billion was spent in this gigantic effort to rebuild both human bodies and national economies. The expenditure continues, not because we can afford it but because we cannot afford to withhold it. The Department of State seems willing to go along cautiously with a program of humanitarian helpfulness for its own sake, but of course it is impossible to divorce the program from the exigencies of international politics. Many purists disapprove of using food — the gift of Earth — for political purposes. At the atavistic roots of this ancient conception, revived a generation ago by Rudolf Steiner, are theories of a mystical relationship between Man and Earth, which once soiled by dishonor, impairs the alleged symbiosis. Today, quick logical thinking is all that we expect from our leaders and we are happy to receive as much. In a word, the cold war has become an imminent threat to civilization, and if we value freedom, we must place *taboo*, in all its forms, in the archives where it belongs.

The problem of successful world nutrition presents itself

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to us as a realistic struggle against time. Unfortunately it is not a simple problem but rather the most stupendous difficulty yet to enter human consciousness. Its ramifications are partly suggested by the fact that we do not yet know, with any degree of precision, where shortages exist, the nature of these shortages, what can be expected from improved agricultural methods, how waste can actually be reduced, how farmers are to produce the right crops for a hungry world, how fertile areas in the tropics can be opened to transportation, how industry can produce in quantity such valuable food as yeast concentrates, or even how the people of India, for example, can be taught the value of the ground nut (peanut) for its remarkable nutritive properties (high protein, high nicotinic acid).

The first element of any feeding program is to ensure calories as a broad protection against fatal inanition. The second element is to ensure against selective starvation and involves supplying the various vitamins, minerals and amino acids, whose serious lack invites the development of such nutritional diseases as beri-beri, pellagra, xerophthalmia, anemia, cirrhosis of the liver and many other disorders. In China, even in areas where sufficient calories are obtainable, there is a high incidence of nutritional diseases, showing distinct differences in various geographic sections, depending upon nearness to the ocean or temperature and sunlight intensities. In India similar conditions are found with perhaps a more widespread lack of calories in the poor rural areas, while the whole national situation is rendered more acute by problems growing out of India's recent liberation. The post-liberation warfare was associated with mass migrations requiring internment camps for persons ill, lost or in transit. While the Indian medical profession, trained in Western science, are, doing all in their power to combat malnutrition and such associated scourges as malaria, they have few supplies to work with, and are hampered by reactionary government elements bent on converting from the scientific, to the indigenous systems of medicine, particularly the ancient Ayurveda. In a country where the dung of the Sacred Cows is used largely for fuel instead of fertilizer and where Hinduism has placed a rather strict religious interdiction on the eating of meat, it is little wonder that the scientific investigator recoils in discouragement from his attempts to improve the nutritional status of the people.

It is in the poorest areas of China and India that the greatest population increases occur. It is precisely here that one should go if he desires to rid himself of all qualms connected with the idea of birth control. Regardless of his previous opinions, or even his religious training, he would feel amid the suffering and death from starvation that any measure would be justified which might partially alleviate such tragedy. He would feel that a child had better not be born than born to early, grim and inevitable disaster. There is nothing on earth half so unjust or pitiable as a child dying from lack of food. The spectacle of such a death is an argument to end all arguments against the need of birth control under such hopeless circumstances, but again, it is precisely here in semibarbarous societies that birth control is almost impossible to establish. Is contraception an absolute wrong or has it a relative application? This is indeed the question that governing bodies may sometime be required officially to answer. Many of the authorities who have devoted the greatest time and study to the problem of the world's food supply are convinced that more and more as time progresses birth control is the only practical solution of the puzzle.

Professor Anton J. Carlson, one of our most renowned physiologists and biological thinkers, in referring recently to the major food predicament confronting the human species now and increasingly in the next 500 years, predicted an unavoidable dysbalance between the factors of nutrition and population, and regarded birth control by some means as ultimately inevitable if we are to avoid disaster. Viewing the prospects as an anthropologist, and accepting war as a violent and undesirable means of reducing population, he did not believe that either war or disease could diminish the number of living persons as rapidly as medical science and natural fertility would cause it to increase. (He did not recommend euthanasia for the aged, which though less acceptable, might seem equally logical.) Dr. Carlson is well aware that the repression of life at its source will never become really popular despite the clarity of scientific opinions but of course in a sense this is of no more importance

than the fact that conscription in wartime will never be popular either.

Dr. Carlson may possibly be on somewhat uncertain grounds in assuming that armed violence could not reduce the human family sufficiently to obviate the menace of mass starvation. There is no good way to know the results of future wars, but at least war appears to have become a fixture in the life of *homo sapiens*, and must be recognized as a biological characteristic of man, most difficult to eradicate. Both slaughter and post-bellum economic stress exert a profound influence on the vigor of participating nations. Civilization was not completely destroyed by our two World Wars, largely because in each instance hostilities were brought rather speedily to an end. Granting that a future war might be greatly prolonged, it could easily have a disastrous effect on global population for centuries to come. This possibility seems to constitute a reason for hesitating before deciding on the inevitability of birth control measures on an unprecedented scale.

Neither should it be thought that we have completely tapped the dietary possibilities within our reach. Universal emphasis on cereal as opposed to animal protein, while not in line with present concepts of excellent nutrition, would render survival possible for a larger number of people than our current use of grain for stock feeding. Eight pounds of grain are required to make one pound of meat but there is no comparison between the caloric value of the two quantities in question. Meat is nutritionally preferable because of the excellent "biological" quality of its proteins, containing as they usually do all the "essential" amino acids. Yet no one can be so stupid as not to recognize that many persons — though not all — who subsist on meatless diets remain healthy, vigorous and productive. No doubt future investigations will of necessity be directed to the point in question, based on broad feeding experiments of human beings. At the moment, the cereal diet, supplemented by small quantities of meat, gives promise of good results provided that the two kinds of food are eaten at the same meal.

Neither should it be too incautiously assumed that, just because medical science is playing an important role in reducing mortality rates, that it is also significantly increasing birth rates. The opposite is almost sure to be the early result. Medical science, sanitary engineering and general hygiene have combined to produce an extension of life expectancy but with the creation of societies of old men and women, who, having long outlived their reproductive periods constitute a growing economic strain upon states and nations. This "load of age" will, in itself, exert a dampening effect upon reproductivity in the younger age groups. Human breeding is especially sensitive to economic environment and as conditions deteriorate in parallel with our over-population in the high age brackets, the birth rate may be relied upon to fall, as it always does in civilized countries under financial pressure. This of course is not true in barbarous areas.

In spite of these comments, Dr. Carlson may indeed be right. Among our peculiarities as human beings are aspirations, inbred respect for ancient custom, and a vigorous faculty of never doing anything until forced to. We are thus in perfect character as we proceed with our breeding, our waste of food and soil and with no thought of what our progeny, five centuries hence will think or even eat. In recommending birth control, Dr. Carlson is well aware that the subject is one to which many persons are extremely sensitive, and hence we must admire his courage. If it were true that the climax of this human nutritional problem were as distant as Dr. Carlson suggests, we might be inclined to feel that his remedy was too drastic as a mere prophylactic. The majority of scientists believe that a serious food impasse is much closer in time, and is indeed already upon us.

Meanwhile, Britain's austerity program is our most familiar reminder of the disharmony now existing in the world's food supply. Dr. John Yadkin, Professor of Physiology at the University of London, recently concluded that so long as world food production and international distribution continue as they are, Britons must continue with a system of rationing and price control. He stated that in the United States alone, 8000 acres of land are daily being lost by soil erosion. In 50 years he expects the population of Asia to reach a figure approaching the present population of the entire world. He recommends contraceptive techniques but despairs of their effectiveness in communities where living conditions and educational levels are very low. He thinks that the solution may lie

in the discovery and use of new principles of birth control as recently hinted by Lord Horder, a British medical leader. It is true enough that the most reliable means of lowering birth rates is by increasing culture, but the processes of civilization and cultural indoctrination set their own pace,—one much too slow to help us in our present problem.

On the one side we have the technical nutritionists and their conferees in the United Nations organizations admitting that the food problem is not only acute but devastating in its implications, yet hoping that means may be discovered of solving it without resort to birth control. On the other side are many bold spirits whose honest convictions prompt them to warn us of the grave dangers ahead which can only be averted by controlling population increase.

The reaction of the man in the street is to wait and see, and trust that, in a few generations our chief worry may be a seriously declining birth rate, induced by natural causes.

We do not require crystal-gazing to realize that the food-population riddle, in its long-term aspects is beginning to present us already with material for the most serious reflection and action. No sizable impression can be made upon this problem in the near future. In our present act of temporizing with it, we see the bizarre spectacle of socialistic and

communistic nations looking hopefully to the last surviving capitalistic nation for help. Inasmuch as liberty is more valuable than food or life, we must become increasingly aware of the erosive influence of socialism and communism upon our ideals and economy. A drastic contest seems bound to occur between the opposing forces of liberty and enslavement decades before any valid solution of the world food crisis is possible. A present realistic attitude is one of food helplessness and general assistance, specifically to those nations who have signified their intention of resisting communism. Under the existing tensions of international politics it appears almost wasted effort to dilute our effectiveness by pouring food, wealth and technological information into those areas where communism meets no real opposition or receives a welcome. Why not concentrate our present efforts definitely to the signers of the North Atlantic Pact? This seems to be a fair appraisal of the fundamental purposes of our own State Department with respect to the world nutrition problem.

Beyond politics, there remains a world-wide scope for ingenuity and heroism, and a vital issue of unprecedented significance, which has within it the power of deeply altering our attitudes toward existence, of visiting slow disaster upon us, or,—let us trust,—of furnishing new victories for human courage and intelligence.

BOOK REVIEWS

DIFFERENTIAL DIAGNOSIS OF INTERNAL DISEASE. Julius Bauer, M. D., F. A. C. P., 866 pages, Grune and Stratton, New York, 1950.

Bauer writes in an informal, almost conversational manner as he examines first the symptoms and then the chief signs of disease. For example, there are 20 pages on headache. Systematic descriptions of disease of the respiratory, cardiovascular, digestive, hemopoietic and urinary systems are utilized. One gains the impression of a teacher speaking somewhat at random from the richness of his own personal experience. Short case histories are thrown in frequently to illustrate points under description. There is a pleasant absence of tabular material. Too much stress is not laid upon laboratory data. The book possesses a strong clinical flavor and also the authoritativeness of a genuine monograph. There are not too many points upon which Bauer departs from conventional acceptances, yet the style and philosophy of the book betray the rugged individualism of a medical thinker who treasures the time-proven value of physical examination and regards the laboratory at least as helpful. The psychosomatic aspects of medicine must be mastered by the internist and practitioner, because 30 percent of practice is based on cases presenting no organic disease. Those who enjoy the thoughtful presentation of personal experience and conviction will regard this text as an important contribution to medicine.

DIABETES GUIDE BOOK FOR THE PHYSICIAN. American Diabetes Association, Inc., 11 W. 42nd St., New York 18, N. Y., 1950.

The Committee on Education of the American Diabetes Association has written and published the title volume of 80 pages for the exclusive use of physicians to enable them to improve their methods in the diagnosis and treatment of diabetes mellitus and its complications. The easy calculation of diets and the preparation of flexible meals is presented in admirably simple form. Complete control of glycosuria and hyperglycemia as well as the exact regulation of body weight are advised in early diabetes, in the initial treatment of diabetes in childhood and in diabetes associated with adiposity. However, less than ideal control may be tolerated in the presence of an unstable blood sugar, when it becomes impossible to keep the urine constantly sugar free and sometimes when treating diabetes in the aged. This represents an enlightened attitude with which nevertheless, certain purists may disagree. The volume is an extremely useful and valuable one, not only because of its immediate utility value but because, in summing up the opinions and attitudes of those specialists nearest to the subject, it gives the impression—which is actually true—that diabetes is a disease easily diagnosed and easily treated with pronounced success.

GENERAL ABSTRACTS

STEVENSON, C. A. AND YATES, C. W.: *Accuracy of roentgen diagnosis of benign gastric ulcer.* (Radiology, May 1949, Vol. 52, No. 5, 633-641).

In a series of 91 adequately followed gastric ulcer patients, the roentgen report of a benign lesion was accurate in 93.4 percent. However, there is no way to differentiate a gastric cancer from a benign ulcer by means of x-ray examination. It might be advisable to operate at once on all cases of x-ray diagnosed gastric benign ulcer in the hope of early removal of the cancer in the approximately 10 percent of cases in which the diagnosis is wrong.

HALLIGAN, E. J., PERKEL, L. L. AND CATLOW, J. K.: *Duodenocolic fistula.* (Am. J. Proctology, 1, 1, 1-16).

Most cases of duodenocolic fistula result from malignant growth of the hepatic flexure or proximal portion of the

transverse colon. Ulcerative colitis may be responsible through perforation. The condition is rare. The second portion of the duodenum most frequently is involved. Sudden intense diarrhea, fecal vomiting and the development of a severe, macrocytic anemia with the loss of the intrinsic factor, are important features of the disease, which may be mistaken for sprue. Diagnosis is made by barium enema. A few cases will respond favorably to radical resection and anastomosis of the second portion of the duodenum. This is particularly useful in benign cases.

ROKA, G., AND LAJTHA, L. G.: *Abolition of pyloric spasm by orally administered procaine solutions.* (Brit. Med. J., May 20, 1950, 1174-76).

The oral administration of 50 to 100 c.c. of a 1 percent solution of procaine, causes the pylorus to open and remain open for some hours. It may be given twice daily for several

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days without side-effects and is recommended as a simple therapeutic procedure in functional pylorospasm and as a preparation for surgery in organic pyloric obstruction. Procaine is more effective than atropine or papaverine, and apparently owes its action to an influence on the local nerve endings.

STROM, J.: *Methionine in the treatment of acute hepatitis.* (Brit. Med. J., May 20, 1950, 1168-1169).

The author used methionine in the treatment of 125 slight and semi-severe cases of acute hepatitis, with an equal number serving as controls. In the cases receiving methionine, bilirubinemia showed less increase and a quicker return to normal, but a marked effect is scarcely to be expected from the use of methionine in acute hepatitis of average severity. In more severe cases, clinical experience suggests that amino acids may be of value when given intravenously.

BARTLEY, C. W.: *Steatorrhea in a family.* (Brit. Med. J., May 20, 1950, 1161-1164).

The author describes steatorrhea occurring in a father, 48, the oldest daughter, 22, and three of five other younger children. Attention was drawn to this family by the discovery of anemia in 4 of the children. In the 5 cases of steatorrhea there was suggestive evidence that varying degrees of fibrocystic disease of the pancreas were present. This was by no means definite. Against it was the fact that one of the children had lived to 22 years of age, while most cases of fibrocystic disease are dead before the age of 15.

DAVIDSON, L. S. P. and FOUNTAIN, J. R.: *Incidence of the sprue syndrome.* (Brit. Med. J., May 20, 1950, 1157-1161).

The unique opportunity afforded by priority food rationing in Britain since 1940 enabled the authors to study certain features of clinical interest in 2,044 cases of the sprue syndrome, consisting of 1303 cases of celiac disease, 403 cases of tropical sprue, 311 cases of idiopathic steatorrhea and 27 unclassified cases. Each year in Great Britain 117 new cases of celiac disease and 44 cases of idiopathic steatorrhea develop. Males and females are equally affected in both diseases. In 34 percent of cases of the idiopathic syndrome, the history suggested that the disease began in childhood. Army statistics on tropical sprue indicated that the prognosis, as it affected personnel in the 1934-45 war was extremely good. In a number of families two or more relatives were affected either by idiopathic steatorrhea or celiac disease, thus suggesting that the genetic factor may be important.

OWEN, J. G. and STONE, C. S.: *Endometriosis of the bowel.* (Bull. Mason Clin. III, 4, 20-27).

When endometriosis of the bowel causes obstruction, resection usually is needed. Small endometrial foci should be eradicated before their continued growth forces the surgeon to perform castration to control the growth. The driving influence of the ovarian activity on the ectopic growths requires either a diminution of that activity or removal of the growths. In younger women with proper pre-operative diagnosis of intestinal endometriosis, the bowel can be prepared and resected where feasible, thus sparing the ovaries. In older women, castration produces satisfactory resolution of all but the most highly obstructive bowel lesions. Castration by x-ray is likely to injure the intestines.

KELTY, R. H., BAGGENSTOSS, A. H. and BUTT, H. R.: *The relation of the regenerated hepatic nodule to the vascular bed in cirrhosis.* (Proc. Staff Meet. Mayo Clin., 25, 2, 17-26).

By the study of a wax reconstruction model of a piece of atrophic nodular liver, it was discovered that the narrowing of the smaller vessels and their obliteration are caused mainly by the pressure of growth and expansion of the regenerated nodule against the rather rigid connective tissue surrounding, between which and in which the vessels are found.

WILLIAMS, A. W.: *The stomach of the recently deceased.* (Brit. Med. J., Jan. 14, 1950, 102-104).

Williams examined 72 unselected stomachs postmortem, formalin-fixed according to Magnus's rulings. (The fixative was usually introduced into the stomach by a stomach tube 45 minutes after death — a procedure which Williams admits may be regarded by some as a "ghoulish business").

By careful histological examination of these stomachs he found that the severity of chronic gastritis tends to increase with age. Uremia seems always to associate itself with chronic gastritis, though the reverse of this statement is not true. Ulceration was found in 15 per cent of adults though never diagnosed during life.

MACLEAN, A. B.: *Primary torsion of the omentum in children.* (Brit. Med. J., Jan. 14, 1950, 100-101).

Three cases of omental torsion are reported as cause of acute abdominal symptoms in children. The rarity of the condition in children presumably is due to the poorly developed omentum in the small child. The cause of torsion is unknown and diagnosis is unlikely before laparotomy. The treatment is simple and consists of resection.

MERIKANGAS, U. R.: *Hyperthyroidism: diagnosis and treatment.* (U. S. Armed Forces M. J., 1, 1, 1-11).

The author advises wider use of the protein-bound blood iodine estimation in the diagnosis of hyper- and hypothyroidism. He is somewhat undecided as to the relative merits of medical and surgical treatment.

HARRIS, F. C. and BYRNE, E. T.: *Extrusion of redundant gastric mucosa into the duodenum.* (U. S. Armed Forces M. J., 1, 1, 12-21).

Among the symptoms produced by extruded gastric mucosa are upper abdominal distress and fullness, vomiting, bleeding and weight loss. The diagnosis is made by x-ray studies. Thirty examples were found among 1000 patients, and 9 cases were treated with excellent results by excision of the extruded mucosa with pyloroplasty.

EISENFELD, O., YOUNG, V. M. and YOSHIMURA, T.: *A survey of salmonella organisms in market meat, eggs and milk.* (J. Amer. Veterinary Med. Ass., 116, 874, 17-21).

All 1000 samples of pasteurized grade A milk examined were found free from Salmonella. Of 512 samples of beef, only one yielded the organism. Three per cent of dried egg powder was positive. 10.8 per cent of uninspected poultry birds were positive, but only 0.9 per cent of U. S. inspected birds. Salmonella strains were isolated from 14.3 per cent of the 573 U. S. inspected and passed pork samples and from 26.8 per cent of uninspected pork. Of hamburger samples, 17.6 were positive.

HALSTEAD, J. A.: *Gastrointestinal disorders of psychogenic origin: management in forward areas.* (Bull. U. S. Army Med. Dept. Nov. 1949 (Supplemental number, — Combat Psychiatry, 163-180).

Gastrointestinal disorders constituted the largest single group of psychosomatic disabilities among American soldiers in World War II. The primary mission of the Medical Corps is the preservation of effective manpower, and not exhaustive medical investigation. It is necessary to be able to recognize illnesses that have no organic basis or cause without delay and to reassure the patient, and prevent him from getting into a hospital with an organic diagnosis.

WRIGHT, A. D. ET AL.: *Discussion on prolapse of the rectum.* (Proc. Royal Soc. Med., XLII, 1005-1016).

Wright states, "Adult sufferers (from rectal prolapse) generally retire from all contacts with the outer world and live the life of social outcasts, and the opportunity of the surgeon to help them is heaven-sent, provided a good method of treatment is employed." Some 36 methods of treatment have been extensively employed, of which the following five are chiefly used in Britain: (1) excision of the pile area in cases in which the prolapse is simply mucous membrane; (2) the anal tightening operation of Thiersch for lesser degrees of true prolapse; (3) the ligature method over a rubber tube for strangulated cases; (4) the rectosigmoidectomy operation of Miles; (5) the pelvic obliterating operation of Moschowitz. The Thiersch operation is rapidly gaining favor. Operative mortality in all methods is low but the recurrence rate is high. The operation of rectosigmoidectomy probably interferes with the afferent fibers of rectal sensation. Lloyd-Davis has had good results by mooring the rectum to the sacrospinous ligaments by sling sutures of nonabsorbable material, at the same time fastening the rectum to the vagina by sutures.

DONACH, I. AND PELC, S. R.: *Autoradiographs with radioactive iodine*. (Proc. Royal Soc. Med., XLII, 12, 957-959).

After injecting radioactive iodine, I^{131} , into a rat, a thin section (5 microns) of the animal's thyroid gland is covered by a closely attached strip of developed photographic emulsion 3 microns thick. Concentrations of blackened photographic grains indicate the presence and position of radioactive material in the underlying tissue, and the slide may be examined under the microscope. During the nine days following the injection, the I^{131} disappears first from central follicles though still present in the peripheral ones. Thyroids of rats given thiouracil before or together with I^{131} failed to produce autoradiographs. Successful autoradiographs were obtained from the human thyroid following the administration of 2 to 100 microcuries of I^{131} by mouth 24 hours before thyroidectomy, provided the patient had received no previous iodine therapy.

MONTGOMERY, A. E.: *Clinical pathological conference*. (Bull. U. S. Army Med. Dept. IX, 11, 934-942).

Assisted by G. T. Patrick, H. T. Berwald, G. S. Dean, A. J. French and A. A. Humphrey, Col. Montgomery presented the case of an officer, 33 years of age, who in Japan was treated for hookworm, but noted persistent diarrhea from that time onward, which caused him a loss of 25 pounds in the next 10 months. At that time, apart from vague abdominal distress and dehydration, a complete examination revealed nothing. A year from the beginning of his illness a second complete examination showed hypoproteinemia, and x-ray revealed several loops of distended small intestine.

A surgical consultant diagnosed chronic peritonitis with secondary ileus of unknown origin. Hydration, vitamins and penicillin as well as whole blood transfusions produced marked improvement, but persistent diarrhea even led to a suspicion of amebiasis. The therapeutic test was made, but the patient at this time became irrational, deteriorated and died approximately a year from the time of his first symptoms. Montgomery had made a diagnosis of regional ileitis and this was confirmed at autopsy, which also showed peritonitis resulting from multiple perforations of the ileum, a congenital Meckel's diverticulum and very marked mesenteric adhesions. By the time a clinical diagnosis was possible, the patient obviously was not a suitable subject for a small bowel resection. The case illustrates the protean manifestations, the surreptitious onset and the confusing clinical picture which regional ileitis usually presents.

BRICK, I. B.: *Primary malignancy of the liver*. (Amer. Practitioner, May, 1950, 475-479).

Primary cancer of the liver may be found at any age but usually in middle-aged men. The Chinese, Japanese and Bantu are particularly susceptible. Commonly it is found associated with cirrhosis, hemochromatosis and fluke infestation. Hepatoma is three times as frequent as cholangioma. The infrequency of antemortem diagnosis is due to the absence of pathognomonic findings, but the use of needle liver biopsy is increasing the frequency of the diagnosis. The disease is of short duration and treatment is futile.

EDWARDS, H. C.: *Carcinoma of the stomach*. (Brit. Med. J., April 29, 1950, 973-978).

In arriving at a diagnosis of gastric cancer, the history is more important than x-ray, gastroscopy or peritoneoscopy. A person of middle age presenting digestive symptoms for the first time, or presenting an unexplained anemia, ought to be suspected of carcinoma of the stomach and subjected to laparotomy, even though all other investigations have yielded negative or equivocal results. A cancer of the stomach may not grow or metastasize any more rapidly than a breast carcinoma. Ulcers in the pyloric antrum should be regarded as potentially malignant and be operated on. The author notes that in some instances fatal delay in surgery has been due to a negative x-ray report, when a cancer actually was present.

KALLQVIST, I.: *Para-aminosalicylic acid therapy in intestinal tuberculosis*. (Am. Rev. Tuberculosis, 61, 5, 621-642).

Twenty-two cases of radiographically-verified secondary intestinal tuberculosis were treated with PAS. The daily dose

was 9.8 gms. given after meals in divided portions, and treatment was continued 3 months or longer. Side effects were diarrhea (controlled by tincture of opium) and nausea and vomiting in a few cases (controlled by antacids). Complete roentgenographic intestinal regression was obtained in 10 cases, and almost complete in one case. Seven cases showed considerable regression. Of 4 cases in which there was no x-ray follow-up, one is symptom-free and 3 are dead. After a period of 16 months from the commencement of PAS treatment, 13 patients were entirely symptom-free, 3 had mild abdominal discomfort and 5 were dead. In all 5 fatal cases (one of which was due to acute monocytic leukemia) subjective improvement was noted following treatment.

GIBB, W. T.: *Some considerations in the differential diagnosis of chronic diarrhea*. (Amer. Practitioner, May, 1950, 480-486).

A chronic diarrhea usually is due to functional upset of the colon, but such a diagnosis ought not to be made until an exhaustive clinical, proctoscopic and radiological examination has ruled out organic lesions, particularly colonic or rectal cancer. Chronic ulcerative colitis, regional enterocolitis, tuberculous enteritis and fecal impaction should be considered. Achylia alone probably seldom causes the so-called gastrogenous diarrhea. Steatorrhea, including the idiopathic form, tropical and non-tropical sprue and celiac disease in children usually are associated with diarrhea. Carbohydrate intolerance is a common cause of diarrhea in older women. Hyperthyroidism, amebic colitis and bacillary dysentery require exclusion. Gastrointestinal allergy, in the author's experience is not usually associated with diarrhea.

WILBUR, D. L. AND WATTS, M. S. M.: *Peptic ulcer: modern criteria for diagnosis and attempted diagnosis of healing*. (Radiology, June 1949, Vol. 52, No. 6, 800-809).

Here is a paper of a moderately nihilistic type which does the mind and soul of a hard-working internist much good! The clinical diagnosis of peptic ulcer depends on the history. A typical ulcer history is accurate in 80 to 95 percent of cases. Radiological diagnosis is said to be 95 percent accurate, too, and must find a niche or deformity. When there is a discrepancy between the clinical and radiological findings, the clinician has to thrash the matter out himself. There is no satisfactory clinical evidence of healing of an ulcer. Radiological evidence for healing also is unsatisfactory.

DAILEY, M. E.: *Gastroscopy in the evaluation of patients with peptic ulcer*. (Radiology, June 1949, Vol. 52, No. 6, 796-799).

Gastroscopy is of diagnostic aid in ruling out associated gastric disease when duodenal ulcers are suspected of causing chronic bleeding or obstruction, or when response to treatment is poor. Benign gastric ulcers may be rather accurately differentiated by gastroscopy from malignant ulcers, but proof of benignity of a given ulcer is established only when gastroscopy shows absolute healing. Significant gastritis or jejunitis may be found gastroscopically in postoperative stomachs when no roentgen signs of disease are evident.

LORIMER, W. S.: *Bleeding peptic ulcers: report of 368 cases*. (Texas State J. Med., 45, 10, 702-706).

Of 80 proven cases of bleeding ulcer in which the hour of onset of bleeding could be determined, about three-quarters occurred during the interdigestive period from 8 p.m. to 8 a.m. This emphasizes the advisability of the 24 hour regimen in treating all active ulcers. The author uses atropine liberally, also suction and blood transfusions and if surgery is necessary, he attacks the bleeding point rather than proceeding with a resection.

BOHN, G.: *Hematemesis as a surgical problem*. (Brit. Med. J., Sept. 17, 1949, 630-633).

33 patients with hematemesis were treated surgically with 2 deaths. At the Royal Berkshire Hospital at Reading, all patients who are bleeding are treated (medically or surgically) in the surgical wards. Surgery can only be justified if a low surgical mortality rate can be obtained, and this depends upon careful selection of cases, efficient transfusions and early laparotomy.

STEEL CAN KNOW-HOW IS GIVEN INDUSTRY BY AMERICAN CAN COMPANY

A major step forward in freeing this country from dependence on foreign sources of can-making materials was demonstrated recently by the American Can Company when it revealed to the industry its process for producing a virtually tinless tin can.

Before representatives of some 90 can manufacturing firms from all parts of the country, American Can officials conducted a formal showing at Proviso plant in Maywood, Ill., of the techniques the company has developed for making an enameled steel container. The only tin used was three per cent in the thin strip of solder which seals the side seam of the can.

Most cans in general use today, it was pointed out by Dr. B. S. Clark, director of research for American Can, are made of light steel plate to which has been applied a thin coating of tin. In Canco's new process, an organic coating of domestic manufacture substitutes for tin in protecting the steel base and the contents packed in the can, he added.

The company's process makes possible a saving of more than 92 per cent of the tin normally used in the manufacture of several large-volume sizes of cans, according to Dr. R. W. Pilcher, manager of American Cans general research laboratories at Maywood.

The demonstration was part of the company's announced policy of making available to the industry the proven results of its continuing research program called "Operation Survival." Planning began in 1946 and the program has been under way actively for the past year. It is aimed at developing containers made entirely from materials available on this continent. Most of the world's tin supplies today come from Malaya and Bolivia, with other foreign countries as additional sources.

The research is being conducted by American Can in conjunction with more than 20 other leading American companies who are potential suppliers of alternate can-making materials.

In announcing the scientific project, W. C. Stolk, Canco's executive

MARCH, 1951

vice president, said the proven findings would be turned over to other can manufacturers as a public service.

The industry group on the plant tour inspected a can-making line which has been converted for the production of the steel cans. The tour included a step-by-step trip along high-speed automatic machines which turned out cans at some 330 a minute.

Cans produced at the demonstration were of the size normally used for pet foods. This type of container, however, is adaptable to the packing of a variety of dry products, such as ground coffee, and some liquid products. The latter include motor oil and anti-freeze.

Preceding the plant inspection visit, the group heard in detail the technical and mechanical aspects of making steel cans with low tin solder. The problems which had to be overcome and the history of the exhaustive research since 1936 that went into the development of the process were described during a morning session.

Speakers at the session included Dr. Clark; Dr. D. E. Wobbe, director of the engineering group at the Maywood laboratories, and C. F. Heiberger, assistant manager of manufacture for the central division.

Others taking part in the discussions were Nels Geertsen of the company's manufacturing department, and R. C. Rosecrance and H. Ferris White, president and executive vice president respectively of the Can Manufacturers' Institute, and representatives of the Quaternary Food and Container Institute in Chicago.

In announcing its "Operation Survival" program, the company pointed out that before World War II solder used in container manufacture contained approximately 40 per cent tin. Continuing research since that time has made possible the reduction of tin content to an average of less than eight per cent and to a low of three per cent, as was demonstrated.

The steel can is another step in the industry's effort to conserve tin. The World War II conservation research, which is being intensified now, resulted in the development of electrolytic plating of steel sheets, which reduced the average amount of tin in a base box of plate (sufficient for approxi-

mately 400 No. 2 cans) from 1.43 pounds to .82 pounds.

It was pointed out that the industry used 41,000 gross tons of tin to make 25 billion cans in 1941, compared to 1950 usage of 31,000 gross tons to make 33 billion cans.

NOTICE

The Michael Reese Hospital Postgraduate School will be offering a two-week intensive course in "Recent Advances in Internal Medicine." This full-time course will meet from April 30th to May 12th, 1951. Clinical and didactic material will be presented by members of the Department of Internal Medicine, other Clinical Departments and of the Division of Laboratories and Research. For further information, address Dr. Samuel Soskin, Dean, 29th Street and Ellis Avenue, Chicago 16, Illinois.

NOTICE

SUB-SPECIALTY BOARD IN GASTROENTEROLOGY OF THE AMERICAN BOARD OF INTERNAL MEDICINE

The names of the following candidates were certified in Gastroenterology, December 11, 1950, at Buffalo, New York:

George R. Boylston, M.D., the Portland Clinic, 1216 S. W. Yamhill street, Portland 5, Ore.

Frank B. McGlone, M.D., 1820 Gilpin street, Denver 6, Colo.

Max Caplan, M.D., 219 W. Main street, Meriden, Conn.

PROMETRON

Manufacturer: Schering Corporation, Bloomfield, New Jersey.

Active constituents: Each cc. contains 2.5 mg. estradiol benzoate U.S.P., and 12.5 mg. crystalline progesterone U.S.P., in oil solution for intramuscular injection. Indications: Treatment of secondary amenorrhea of short duration due to endocrine deficiency. In most cases, uterine bleeding will occur in from three to six days after the last injection. Dosage: One cc. intramuscularly, followed the next day by the same dose. The complete treatment is two injections. Packaging: Available in single boxes of two 1 cc. ampules, and in packages of three boxes. Now also available in 10 cc. vials, in boxes of one vial and six vials.

ANNOUNCEMENT

A course in the theory and techniques of autoradiography will be held this summer by the Special Training Division of the Oak Ridge Institute of Nuclear Studies. George A. Boyd, who is well-known for his work in this field, will direct the course, which will begin on July 2 and continue for from three to four weeks.

Subjects to be covered in lectures and laboratory sessions will include:

a. Theory of the photographic process.

b. Reaction of ionizing particles with photographic emulsions and the interpretation of results.

c. Techniques of making gross and microscopic autoradiograms, including special histological procedures such as freeze-drying, carbowax embedding and smearing of cell suspensions on emulsion surfaces.

The course is intended for professional research workers who will direct research employing auto-

radiographic techniques. Applicants must have completed the basic radioisotope techniques course given by the Institute or possess equivalent experience in the use of radioisotopes in medical or biological research. Twenty individuals from the medical and biological sciences will be accepted for the course.

Lecturers and laboratory leaders will include:

Julian Webb and John Spence, Eastman Kodak Company.

Robert Dudley, Massachusetts Institute of Technology.

Margaret Holt, New England Deaconess Hospital.

C. P. Leblond and Rita Bogorach, McGill University.

L. F. Belanger, University of Ottawa.

S. R. Pelc, Hammersmith Hospital, London.

Agnes Williams, University of New Mexico.

Harvey Blank, University of Pennsylvania.

Registration for the course will be \$25.00.

Additional information and application forms will be available at a later date from Ralph T. Overman, Chairman, Special Training Division, Oak Ridge Institute of Nuclear Studies, P. O. Box 117, Oak Ridge, Tennessee.

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PRODUCTION OF ARALEN SOARS

New Antimalarial Replaces Atabrine of World War II as Chief Weapon Against Malaria for U. S. Forces

Production of Aralen, the anti-malarial which has taken the place of Atabrine in use by American armed forces, has tripled since Korean hostilities began and will be stepped up another 140 per cent by July, it was disclosed recently by Dr. Theodore G. Klumpp, president of Winthrop-Stearns, Inc.

Current output of the product is at the rate of 100,000,000 tablets a year, which will be increased to an annual rate of 240,000,000, he said. Scientists of the Sterling-Winthrop Research Institute synthesized Aralen several years ago.

Aralen is known chemically as 7-chloro-4-(4-diethylamino-1-methylbutylamino) quinoline diphosphate. Clinical investigation has shown it to relieve acute attacks of malaria

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The "Bonus" Action of Chloresium Powder

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2. Prompt antacid action (aluminum hydroxide, magnesium trisilicate)—no alkalosis, no acid rebound, no interference with bowel regularity.

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Now—results in resistant cases

The minimum known history of the ulcers treated with Chloresium Powder in a recent clinical series* was two years. Many of them had resisted previous methods of treatment for from 5 to 12 years.

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Patients welcomed not only the prompt symptomatic relief but also the unusual freedom which the Chloresium Powder treatment gave them. No special diets were required! There were no restrictions on smoking, alcoholic beverages or daily activity!

We invite you to try Chloresium Powder on your most difficult case. Just mail the coupon today!

*Offenkrantz, W. F., Rev. Gastroenterol, 17:359-367 (May), 1950

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much faster than previously known drugs, and to cure falciparum malaria, a type of disease that is non-relapsing but often fatal.

Every G. I. stationed in the malarious regions of the world during World War II was familiar with Atabrine, nicknamed the "little yellow pill." G. I.'s had to take one tablet (0.1 gram) every day as a suppressive or prophylactic dose. A curative treatment required 28 Atabrine tablets over a 7-day period.

Comparative doses with Aralen, which is a white tablet, are one

tablet (0.5 gram) per week as a suppressive or prophylactic dose, and five tablets over only a 2½-day period for cure, Dr. Klumpp explained. Aralen does not produce temporary discoloration of the skin, as Atabrine did, he pointed out.

Malaria is perhaps the world's most prevalent disease. Varying estimates of its incidence range up to 800,000,000 cases a year, with approximately 3,000,000 deaths.

Atabrine therefore assumed critical importance in the early stages of World War II when the Jap-

anese conquered the Dutch East Indies, source of 95 per cent of the world's quinine, which for 300 years had been the traditional anti-malarial.

The total output of Atabrine in the United States in 1944 reached a peak of 3,500,000,000 tablets. Winthrop-Stearns itself supplied 1,400,000,000 Atabrine tablets, or 140,000,000 grams, as compared with the annual rate for Aralen of 120,000,000 grams which will be attained by July of this year.

Chemical intermediates required for manufacturing Aralen are produced by the Hilton-Davis Chemical Company Division of Sterling Drug Inc., at its plant in Cincinnati. Capacity of these plants has been substantially enlarged through construction and installation of new equipment. From the intermediates, Winthrop-Stearns manufactures Aralen in tablet form as well as in ampuls for injection, at its plants in Rensselaer, N. Y.

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Active Constituents: In each teaspoonful (4 cc.): Trimeton maleate 7.5 mg., ammonium chloride 104.8 mg., sodium citrate 43.0 mg., and chloroform 17.5 mg., in a palatable, cherry flavored cordial base; contains 7% alcohol. Action: Counteracts allergic manifestations of a beginning cold, acts as a decongestant and expectorant, controls cough through sedation of cough reflex. Indications: Trimetose is indicated in the control of coughs due to colds. Dosage: Adults: One to two teaspoonfuls 3 to 4 times a day. Children: 6 to 12 years, one-half adult dosage; under 6 years, as prescribed by the physician. Packaging: Bottle of 16 ounces.

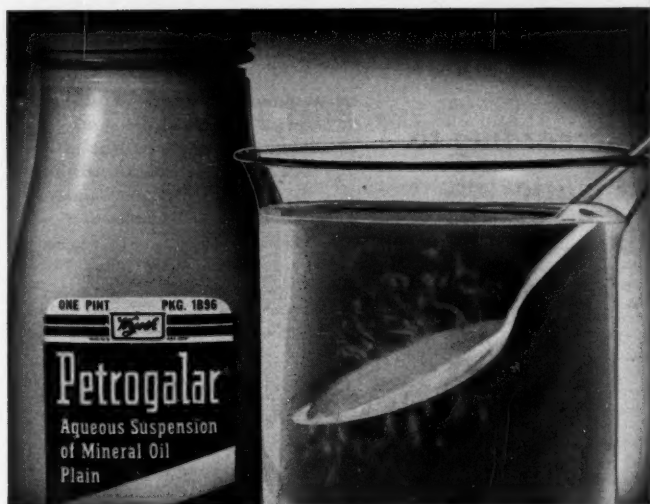
MEDICAL WRITERS PLAN

1951 plans to help expand the membership and influence of the American Medical Writers' Association:

1. The formation of an Advisory Committee consisting of the Editors of the State Medical Journals of the United States who are active members of this Association. They shall elect a Chairman and Secretary, meet with our Execu-

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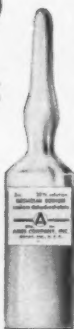
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according to
therapeutic
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In biliary tract disorders, present-day medical management hinges on stimulation therapy and non-surgical drainage. A therapeutic plan is to flush and drain the hepatobiliary tract by increasing the volume of bile while reducing its viscosity, solid content and specific gravity.

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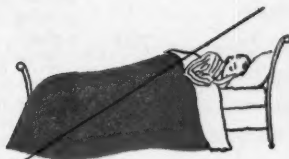
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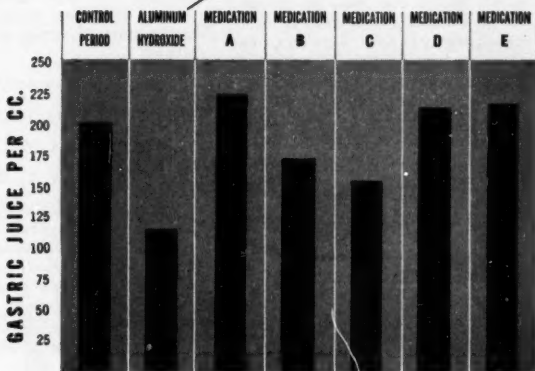


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By taking Creamalin during the day only, the peptic ulcer patient will sleep undisturbed from midnight to morn.

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tive Committee annually and shall advise ways and means of expanding the influence of the Association.

2. A gold medal and a certificate to be known as the "Distinguished Service Award" to be presented annually to a member of the Association who has been an active member for at least five years previously and "who has rendered unusual and distinguished service to the medical profession." Active and life members of the Association may make nominations for this award, sending them to the President or Secretary. Final nominations are made by the Past Presidents (later this may be changed to an Annual Awards Committee, consisting of five members, one member being appointed each year by the retiring Association president, members so appointed to serve for five years) who shall recommend three members to the Executive Committee for election by that group.

3. A gold medal and a certificate to be known as the "Honor Award" to be presented from time to time at the annual meeting to non-Association members who have made distinguished contributions to medical literature. Active and life members of the Association may make nominations for this award, sending them to the President or the Secretary. Final nominations are made by the Past Presidents (later this may be changed to the Advisory Committee in order to stimulate this committee and to give them something specific to do) who shall recommend three names to the Executive Committee for election by that group. Honor Award recipients must be present at the annual meeting to receive the award.

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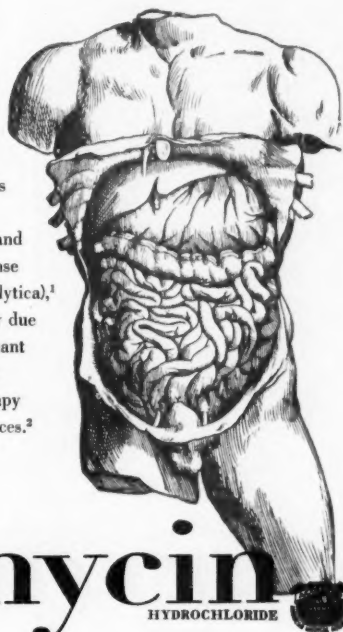
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1. Most, H., and Van Assendelft, F.: Ann. New York Acad. Sc. 53:427 (Sept. 15) 1950.

2. Finland, M.; Gocke, T. M.; Jackson, G. G.; Womack, C. R., and Kass, H.: Ann. New York Acad. Sc. 53:290 (Sept. 15) 1950.

3. Dowling, H. F.; Lepper, M. H.; Caldwell, E. R., and Spies, H. W.: Ann. New York Acad. Sc. 53:433 (Sept. 15) 1950.

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